=> d his

(FILE 'USPAT' ENTERED AT 10:16:53 ON 08 NOV 1998)
E ISNER/IN
L1 8 S E5
L2 0 S L1 AND (ENDOTHEL?)(P)(PROGENITOR? OR STEM)
L3 174 S (ISCHEM? OR ANGIOGEN? OR VESSEL? OR VASCULA?) AND (ENDOTHEL
L4 86 S (ISCHEM? OR ANGIOGEN? OR VESSEL? OR VASCULA?)(P)(ENDOTHEL?)
L5 34 S L4(P)(TREAT? OR THERAP? OR ADMINISTER?)

=> s l3 and (isolat? or purified)(P)(endothel?)(P)(stem or progenitor?)

317451 ISOLAT?
133251 PURIFIED
7150 ENDOTHEL?
87797 STEM
1778 PROGENITOR?
28 (ISOLAT? OR PURIFIED)(P)(ENDOTHEL?)(P)(STEM OR PROGENITOR?)
L6 16 L3 AND (ISOLAT? OR PURIFIED)(P)(ENDOTHEL?)(P)(STEM OR PROGENIT
OR?)

=> d l6 1-16

1. 5,830,678, Nov. 3, 1998, Method for identifying a target peptide that modulates the binding of epinectin ligand to integrin receptors; William Gene Carter, 435/7.24, 7.1, 7.2; 530/395 [IMAGE AVAILABLE]

2. 5,770,420, Jun. 23, 1998, Methods and products for the synthesis of oligosaccharide structures on glycoproteins, glycolipids, or as free molecules, and for the isolation of cloned genetic sequences that determine these structures; John B. Lowe, et al., 435/193, 252.3, 320.1, 325; 536/23.2, 23.4 [IMAGE AVAILABLE]

3. 5,767,252, Jun. 16, 1998, Neuronal cell growth factor, Narp; Paul Worley, et al., 530/399, 350 [IMAGE AVAILABLE]

4. 5,763,156, Jun. 9, 1998, Inhibition of complement mediated inflammatory response; Peter J. Sims, et al., 435/4, 2, 7.1, 7.2, 7.21, 29, 325, 366, 372, 374; 436/821; 604/7 [IMAGE AVAILABLE]

5. 5,744,347, Apr. 28, 1998, Yolk sac stem cells and their uses; Thomas E. Wagner, et al., 435/354, 7.21, 355, 378, 401 [IMAGE AVAILABLE]

6. 5,681,714, Oct. 28, 1997, Nucleic acid encoding tek receptor tyrosine kinase; Martin L. Breitman, deceased, et al., 435/69.1, 194, 252.3, 254.11, 320.1, 325, 352, 358, 365, 367 [IMAGE AVAILABLE]

7. 5,660,825, Aug. 26, 1997, Method of inhibition of complement mediated inflammatory response; Peter J. Sims, et al., 424/130.1, 131.1, 141.1, 158.1, 810; 514/2, 12; 530/387.2, 388.25 [IMAGE AVAILABLE]

8. 5,635,178, Jun. 3, 1997, Inhibition of complement mediated inflammatory response using monoclonal antibodies specific for a

component forming the C56-9 complex which inhibit the platelet or endothelial cell activating function of the C56-9 complex; Peter J. Sims, et al., 424/145.1; 530/388.25 [IMAGE AVAILABLE]

9. 5,635,156, Jun. 3, 1997, Non-lethal methods for conditioning a recipient for bone marrow transplantation; Suzanne T. Ildstad, 424/1.49, 130.1, 141.1, 152.1, 153.1, 154.1, 178.1, 181.1, 183.1; 600/1; 604/20 [IMAGE AVAILABLE]

10. 5,599,703, Feb. 4, 1997, In vitro amplification/expansion of CD34.sup.+ stem and progenitor cells; Thomas A. Davis, et al., 435/373; 424/93.7; 435/385, 386 [IMAGE AVAILABLE]

11. 5,573,940, Nov. 12, 1996, Cells expressing high levels of CD59; Peter J. Sims, et al., 435/362; 424/93.21; 435/69.1 [IMAGE AVAILABLE]

12. 5,559,022, Sep. 24, 1996, Liver reserve cells; Brian A. Naughton, et al., 435/370; 424/93.1; 435/379 [IMAGE AVAILABLE]

13. 5,550,108, Aug. 27, 1996, Inhibition of complement mediated inflammatory response; Peter J. Sims, et al., 514/21, 2, 8, 12; 530/350, 380, 830 [IMAGE AVAILABLE]

14. 5,514,364, May 7, 1996, Non-lethal methods for conditioning a recipient for bone marrow transplantation; Suzanne T. Ildstad, 424/1.49, 130.1, 141.1, 152.1, 153.1, 154.1, 178.1, 183.1; 600/1; 604/20 [IMAGE AVAILABLE]

15. 5,409,710, Apr. 25, 1995, Foam cell drug delivery; Robert J. Leonard, 424/489, 93.1, 450 [IMAGE AVAILABLE]

16. 5,135,916, Aug. 4, 1992, Inhibition of complement mediated inflammatory response; Peter J. Sims, et al., 514/21, 2, 8, 12; 530/350, 380, 830 [IMAGE AVAILABLE]

=> d l6 1-16 date

L6: 1 of 16

TITLE: Method for identifying a target peptide that modulates the binding of epinectin ligand to integrin receptors
US PAT NO: 5,830,678 DATE ISSUED: Nov. 3, 1998 [IMAGE AVAILABLE]
APPL-NO: 08/643,770 DATE FILED: May 6, 1996
REL-US-DATA: Continuation of Ser. No. 292,065, Aug. 17, 1994, abandoned, which is a continuation of Ser. No. 154,638, Nov. 18, 1993, abandoned, which is a continuation of Ser. No. 654,103, Feb. 8, 1991, abandoned, which is a continuation-in-part of Ser. No. 607,137, Oct. 30, 1990, abandoned.

L6: 2 of 16

TITLE: Methods and products for the synthesis of oligosaccharide structures on glycoproteins, glycolipids, or as free molecules, and for the isolation of cloned genetic sequences that determine these structures
US PAT NO: 5,770,420 DATE ISSUED: Jun. 23, 1998 [IMAGE AVAILABLE]
APPL-NO: 08/525,058 DATE FILED: Sep. 8, 1995

L6: 3 of 16

TITLE: Neuronal cell growth factor, Narp
US PAT NO: 5,767,252 DATE ISSUED: Jun. 16, 1998 [IMAGE AVAILABLE]
APPL-NO: 08/631,607 DATE FILED: Apr. 8, 1996

L6: 4 of 16

TITLE: Inhibition of complement mediated inflammatory response
US PAT NO: 5,763,156 DATE ISSUED: Jun. 9, 1998
[IMAGE AVAILABLE]
APPL-NO: 08/769,382 DATE FILED: Dec. 19, 1996
REL-US-DATA: Division of Ser. No. 465,548, Jun. 5, 1996, Pat. No. 5,660,825, which is a division of Ser. No. 243,540, May 16, 1994, Pat. No. 5,550,108, which is a continuation of Ser. No. 813,432, Dec. 24, 1991, abandoned, which is a division of Ser. No. 365,199, Jun. 12, 1989, Pat. No. 5,135,916.

L6: 5 of 16

TITLE: Yolk sac stem cells and their uses
US PAT NO: 5,744,347 DATE ISSUED: Apr. 28, 1998
[IMAGE AVAILABLE]
APPL-NO: 08/223,902 DATE FILED: Apr. 6, 1994
REL-US-DATA: Continuation-in-part of Ser. No. 90,229, Jul. 9, 1993, abandoned, which is a continuation-in-part of Ser. No. 880,375, May 8, 1992, abandoned, which is a continuation-in-part of Ser. No. 730,250, Jul. 15, 1991, abandoned, which is a continuation-in-part of Ser. No. 4,077, Jan. 16, 1987, Pat. No. 5,032,407, Jul. 16, 1991.

L6: 6 of 16

TITLE: Nucleic acid encoding tek receptor tyrosine kinase
US PAT NO: 5,681,714 DATE ISSUED: Oct. 28, 1997
[IMAGE AVAILABLE]
APPL-NO: 08/278,089 DATE FILED: Jul. 20, 1994
REL-US-DATA: Continuation-in-part of Ser. No. 235,408, Apr. 29, 1994, abandoned, which is a continuation-in-part of Ser. No. 921,795, Jul. 30, 1992, abandoned.

L6: 7 of 16

TITLE: Method of inhibition of complement mediated inflammatory response
US PAT NO: 5,660,825 DATE ISSUED: Aug. 26, 1997
[IMAGE AVAILABLE]
APPL-NO: 08/465,548 DATE FILED: Jun. 5, 1995
REL-US-DATA: Division of Ser. No. 243,540, May 16, 1994, Pat. No. 5,550,108, which is a continuation of Ser. No. 813,432, Dec. 24, 1991, abandoned, which is a division of Ser. No. 365,199, Jun. 12, 1989, Pat. No. 5,135,916.

L6: 8 of 16

TITLE: Inhibition of complement mediated inflammatory response using monoclonal antibodies specific for a component forming the C56-9 complex which inhibit the platelet or endothelial cell activating function of the C56-9 complex
US PAT NO: 5,635,178 DATE ISSUED: Jun. 3, 1997
[IMAGE AVAILABLE]
APPL-NO: 08/207,841 DATE FILED: Mar. 8, 1994
REL-US-DATA: Continuation of Ser. No. 813,432, Dec. 24, 1991, abandoned, which is a division of Ser. No. 365,199, Jun. 12, 1989, Pat. No. 5,135,916, Aug. 4, 1992.

L6: 9 of 16

TITLE: Non-lethal methods for conditioning a recipient for bone marrow transplantation
US PAT NO: 5,635,156 DATE ISSUED: Jun. 3, 1997
[IMAGE AVAILABLE]
APPL-NO: 08/337,785 DATE FILED: Nov. 14, 1994
REL-US-DATA: Continuation-in-part of Ser. No. 120,256, Sep. 13, 1993,

Pat. No. 5,514,364.

L6: 10 of 16

TITLE: In vitro amplification/expansion of CD34.sup.+ stem and progenitor cells
US PAT NO: 5,599,703 [IMAGE AVAILABLE] DATE ISSUED: Feb. 4, 1997
APPL-NO: 08/142,569 DATE FILED: Oct. 28, 1993

L6: 11 of 16

TITLE: Cells expressing high levels of CD59
US PAT NO: 5,573,940 [IMAGE AVAILABLE] DATE ISSUED: Nov. 12, 1996
APPL-NO: 08/271,562 DATE FILED: Jul. 7, 1994
REL-US-DATA: Continuation of Ser. No. 729,926, Jul. 15, 1991, abandoned, which is a continuation-in-part of Ser. No. 365,199, Jun. 12, 1989, Pat. No. 5,135,916.

L6: 12 of 16

TITLE: Liver reserve cells
US PAT NO: 5,559,022 [IMAGE AVAILABLE] DATE ISSUED: Sep. 24, 1996
APPL-NO: 08/378,762 DATE FILED: Jan. 26, 1995
REL-US-DATA: Continuation of Ser. No. 958,621, Oct. 9, 1992, abandoned.

L6: 13 of 16

TITLE: Inhibition of complement mediated inflammatory response
US PAT NO: 5,550,108 [IMAGE AVAILABLE] DATE ISSUED: Aug. 27, 1996
APPL-NO: 08/243,540 DATE FILED: May 16, 1994
REL-US-DATA: Continuation of Ser. No. 813,432, Dec. 24, 1991, abandoned, which is a division of Ser. No. 365,199, Jun. 12, 1989, Pat. No. 5,135,916.

L6: 14 of 16

TITLE: Non-lethal methods for conditioning a recipient for bone marrow transplantation
US PAT NO: 5,514,364 [IMAGE AVAILABLE] DATE ISSUED: May 7, 1996
APPL-NO: 08/120,256 DATE FILED: Sep. 13, 1993

L6: 15 of 16

TITLE: Foam cell drug delivery
US PAT NO: 5,409,710 [IMAGE AVAILABLE] DATE ISSUED: Apr. 25, 1995
APPL-NO: 08/049,943 DATE FILED: Apr. 20, 1993

L6: 16 of 16

TITLE: Inhibition of complement mediated inflammatory response
US PAT NO: 5,135,916 [IMAGE AVAILABLE] DATE ISSUED: Aug. 4, 1992
APPL-NO: 07/365,199 DATE FILED: Jun. 12, 1989

=> d l6 1-16 kwic

US PAT NO: 5,830,678 [IMAGE AVAILABLE] L6: 1 of 16

SUMMARY:

BSUM(23)

The . . . of epithelial tissues as a protective barrier is readily apparent in the body as the lining of body cavities, blood **vessels**, digestive tract, mammary glands, urogenital, endocrine,

reticuloendothelial systems, respiratory surfaces, placenta, and surrounding the nerves and brain. The epithelia also. . .

DETDESC:

DETD(7)

These . . . findings, and on reinterpretation of previous reports in light of the new insights gained from the present invention, namely: (i) **Purified** epinectin induced cell adhesion and localization of the .alpha..sub.3 .beta..sub.1 integrin receptor in focal adhesions better than laminin, fibronectin, or. . . contacts. (iii) In tissue, epinectin localized in most epithelial basement membranes, but not in the basement membranes of muscle, or **endothelium**. At the ultrastructural level, epinectin localized to the Lamina lucida of the epidermal/dermal basement membrane of skin. Consistently, epinectin localized. . . the .alpha..sub.3 .beta..sub.1 integrin receptors in the basal plasma membrane, as well as with the .beta..sub.4 integrin-containing hemidesmosomes of basal (**stem**) cells.

US PAT NO: 5,770,420 [IMAGE AVAILABLE] L6: 2 of 16

DETDESC:

DETD(136)

In . . . between cells of the immune system, and some tumor cells, and the surfaces of the endothelial cells that line the **vascular** tree. These observations suggest the possibility that the cloned fucosyltransferase sequence described here could be used to construct oligosaccharide-type molecules,. . .

DETDESC:

DETD(244)

Oligosaccharides . . . between cells of the immune system, and some tumor cells, and the surfaces of the endothelial cells that line the **vascular** tree. Thus, the cloned fucosyltransferase sequence described here may be used to construct oligosaccharide-type molecules, with pharmaceutical properties possessing anti-inflammatory. . .

DETDESC:

DETD(257)

Five . . . been cloned. Their corresponding enzymes catalyze the formation of various .alpha.(1,3)- and .alpha.(1,4)-fucosylated cell surface oligosaccharides, including several that mediate leukocyte-**endothelial** cell adhesion during inflammation. Inhibitors of such enzymes are predicted to operate as anti-inflammatory agents; in principle, the **isolation** or design of such agents may be facilitated by identifying peptide segment(s) within these enzymes that interact with their oligosaccharide. . . as idiosyncratic acceptor substrate specificities. The in vivo acceptor substrate specificities of these .alpha.(1,3)Fuc-T chimeras, and of their wild type **progenitors**, were determined by characterizing the cell surface glycosylation phenotype determined by these enzymes, after expressing them in a mammalian cell. . .

DETDESC:

DETD(258)

Cell . . . a substantial amount of attention because some are thought

to be essential to the initiation of immune cell adhesion to **vascular** endothelium during the inflammatory process (Reviewed in Feizi, T. (1991) TIBS, vol. 16, 84-86; Springer, T. A., and Lasky, L.. . . . of adhesion mediated by interactions between sialyl Lewis x (sLe.sup.x)-bearing glycoconjugates on leukocytes and P- and E-selectin expressed by activated **vascular** endothelium (Lowe, J. B. Carbohydrate recognition in cell-cell interaction. Molecular Glycobiology. In: Frontiers in Molecular Biology. Fukuda, M. (ed). Oxford. . .

US PAT NO: 5,767,252 [IMAGE AVAILABLE] L6: 3 of 16

DETDESC:

DETD(57)

"Therapeutically . . . not limited to Alzheimer's disease, Parkinson's disease, stroke, epilepsy, neurodegenerative disease, Huntington's disease, and brain or spinal cord injury/damage, including **ischemic** injury.

DETDESC:

DETD(127)

Four . . . molecules is limited and is based primarily on their sequence homology to SAP and CRP. TSG-14 is rapidly induced in **endothelial** cells by growth factor stimulation and is hypothesized to modify the extracelluar matrix of the **endothelium** (Breviaro, et al., supra; Lee et al., J. Of Immunology, 150:1804, 1993). Overall, TSG-14 is 22% identical to Narp but. . . and this domain is predicted to possess a high degree of .alpha.-helical structure. Another pentraxin, termed NP (Neuronal Pentraxin) was **purified** from brain membranes as a binding protein for the sake venom toxin, taipoxin (Schlimgen et al., Neuron, 14:519, 1995). NP. . . sequence is 45% identical to Narp. NP is expressed in discrete populations of neurons in the hippocampus, cortex and brain **stem** indicating a partially overlapping pattern of expression with Narp. The regulation of NP, particularly whether it is an IEG, has. . . glia and is hypothesized to play a role in reputake of extracellular proteins. The third novel pentraxin, termed Apexin, was **purified** and cloned independently by two groups from guinea pig sperm (Noland et al., J. of Biological Chemistry, 269:32607, 1994; Reid. . .

US PAT NO: 5,763,156 [IMAGE AVAILABLE] L6: 4 of 16

ABSTRACT:
A . . . of the C5b-9 complex. The compositions can be used in vitro to inhibit C5b-9 related stimulatory responses of platelets and **vascular** endothelium of perfused organs and tissues, thereby preventing the C5b-9 initiated cell necrosis or stimulated secretion of proteolytic enzymes and. . .

SUMMARY:

BSUM(5)

Recently, the C5b-9 proteins of the human plasma complement system have been implicated in non-lytic stimulatory responses from certain human **vascular** and blood cells. The capacity of C5b-9 to modify membrane permeability and to selectively alter ion conductance is thought to elicit these non-lytic responses from human cells. In the case of human blood platelets and **vascular** endothelium, assembly of the C5b-9 complex initiates a transient and reversible depolarization of the plasma membrane potential, a rise in. . .

SUMMARY:

BSUM(7)

This . . . and coagulation systems at the surface of blood platelets and endothelium can generate inflammatory and chemotactic peptides at sites of **vascular** thrombus formation and may contribute to the altered hemostasis associated with immune disease states. In addition, immune reactions affecting blood. . . and vasoactive amines from platelet storage granules, and increase adherence of platelets and leukocytes to the endothelial lining of blood **vessels**.

SUMMARY:

BSUM(9)

In . . . also adversely affected by the spontaneous activation of the complement system, resulting in membrane insertion of the C5b-9 proteins into **vascular** endothelium. Activation of C5 to C5a and C5b has been shown to be catalyzed by plastics and other synthetic membranes required to maintain perfusion of **vascular** beds during in vitro tissue and organ storage. In addition, membrane deposition of C5b-9 in vivo has been implicated in. . .

SUMMARY:

BSUM(10)

Platelet . . . the subendothelium, which is known to occur in regions of atheromatous degeneration and suggests localized generation of C5a at the **vessel** wall, is potentially catalyzed by adherent platelets and b) local intravascular complement activation resulting in membrane deposition of C5b-9 complexes accompanies coronary **vessel** occlusion and may affect the ultimate extent of myocardial damage associated with infarction.

SUMMARY:

BSUM(17)

The compositions can be used in vitro to inhibit C5b-9 related stimulatory responses of platelets and **vascular** endothelium of perfused organs and tissues, thereby preventing the C5b-9 initiated cell necrosis or stimulated secretion of proteolytic enzymes and. . . the exposure of the procoagulant membrane receptors during collection and in vitro storage. In one variation of this embodiment, the **vascular** endothelium of organs and tissues to be transplanted are treated with these compositions to protect these cells from complement activation. . .

DETDESC:

DETD(2)

37 . . . the studies detailed below indicate that a deletion or inactivation of these cell surface components would increase the risk of **vascular** thrombosis and lead to a decreased storage time for platelets and platelet rich plasma (PRP), and perfused organs and transplanted. . .

DETDESC:

DETD(69)

In this context, it is important to note that affected red cells obtained from patients with the acquired **stem** cell disorder

Paroxysmal Nocturnal Hemoglobinuria (PNH) have been shown to exhibit abnormal sensitivity to lysis by the C5b-9 proteins. This. . . of complement mediated disorders, particularly in view of the discovery that the inhibitor is also found on the surface of **endothelial** cells. As a result, administration of the inhibitor protein, whether **purified** from cells or expressed from cells engineered using recombinant techniques, or portions of the peptide having the same measurable activity,. . .

DETDESC:

DETD(70)

Treatment . . . immune disorders and diseases such as immunovasculitis, rheumatoid arthritis, scleroderma, disseminated intravascular coagulation, lupus, paroxysmal nocturnal hemoglobinuria, thrombotic thrombolytic purpura, **vascular** occlusion, reocclusion after surgery, coronary thrombosis, and myocardial infarction, is accomplished by administering an effective amount of a composition containing. . .

DETDESC:

DETD(73)

In . . . organs and tissue for transplantation, the C5b-9 inactivators would be added to the perfusate or storage medium to protect the **vascular** lining cells from ongoing complement activation during in vitro storage. Additionally, by coating these endothelial cells with a membrane-anchored C5b-9. . .

US PAT NO: 5,744,347 [IMAGE AVAILABLE] L6: 5 of 16

ABSTRACT:
The present invention is directed to mammalian yolk sac **stem** cells. In particular, it relates to the characterization, culturing, long-term expansion and uses of yolk sac **stem** cells for in vivo reconstitution and therapy. Yolk sac **stem** cells **isolated** from the early embryonic yolk sac prior to blood island formation exhibit a homogeneous morphology and a primitive cell surface. . . be induced to express various blood cell markers upon stimulation with specific cytokines. In addition, the cells also express certain **endothelial** cell markers and growth characteristics. Such yolk sac cells may be particularly effective in the reconstitution of a lymphohematopoietic system, as they are capable of forming both **endothelial** cells and blood cells. Therefore, yolk sac **stem** cells may have a wide range of applications including but not limited to the reconstitution of a destroyed or deficient. . .

SUMMARY:

BSUM(28)
6.2.4. **ENDOTHELIAL** GROWTH CHARACTERISTICS OF YOLK SAC **STEM** CELLS

SUMMARY:

BSUM(41)

The present invention is directed to mammalian yolk sac **stem** cells. In particular, it relates to the characterization, culturing, long-term expansion and uses of yolk sac **stem** cells for in vivo reconstitution and therapy. Yolk sac **stem** cells **isolated** from the early embryonic yolk sac prior to blood island formation exhibit a homogeneous morphology and a primitive cell surface. . . be induced to express various blood cell markers upon stimulation with specific cytokines. In

addition, the cells also express certain **endothelial** cell markers and growth characteristics. Such yolk sac cells may be particularly effective in the reconstitution of a lymphohematopoietic system, as they are capable of forming both **endothelial** cells and blood cells. Therefore, yolk sac **stem** cells may have a wide range of applications including but not limited to the reconstitution of a destroyed or deficient. . .

DETDESC:

DETD(2)

The present invention relates to yolk sac **stem** cells, to methods of **isolating** and culturing the yolk sac **stem** cells, and to methods of using the yolk sac **stem** cells. The cells of the subject invention express both primitive hematopoietic and **endothelial** phenotype. In culture, they are able to give rise to **endothelial** tubular structures and mature blood cells. Thus, the yolk sac **stem** cells described herein are a population of pluripotent hematopoietic/**endothelial** **progenitor** cells.

DETDESC:

DETD(7)

Stem cells of the embryonic yolk sac offer particular advantages for hematopoietic reconstitution. Unlike the cells of the embryo, the cells. . . inthe yolk sac begin to form blood islands. The cells of the blood islands differentiate, the peripheral cells becoming the **endothelium** of the futureblood **vessels**, and the central cells becoming first mesenchymal cells and then the red and white blood cells. The blood islands establish. . .

DETDESC:

DETD(14)

Since . . . yolk sac marks the beginning of cellular differentiation and blood cell formation, it is preferable that yolk sac cells be **isolated** prior to extensive blood islandformation. Large numbers of highly homogeneous yolk sac cells of day 7 murine embryos (or similar stage human yolk sac cells), can be **isolated** using the method described herein, and cells obtained at this stage shouldin principle contain the least committed and least differentiated pluripotent **stem** cells suitable for long-term in vitro culture, for use inimmediate in vivo therapy or as carriers of specific exogenous genes for use in gene therapy. In addition, yolk sac cells **isolated** in this manner may contain a relatively homogeneous population of **stem** cells that does not require further purification steps. Thus, most if not all of the cellsmay be capable of differentiating into mature blood cells and **endothelial** cells. This is in contradistinction to the bone marrow derived hematopoietic **stem** cells which are present in minute quantities in the bone marrow.

DETDESC:

DETD(32)

The . . . of the yolk sac cells provide for additional uses. For example, the yolk sac cells may be used for re-endothelization, **vascular** prosthesis and induction of **angiogenesis**. In addition, they may be used as **vascular** grafts, including grafts which secrete tissue plasminogen activator, low density lipoprotein receptor, apolipid protein A, or other biologically active substances.. . .

DETDESC:

DETD(99)

Taken together, the results indicate that the yolk sac **stem** cells possess both hematopoietic and **endothelial** cell phenotypic characteristics.

DETDESC:

DETD(103)

6.2.4. **ENDOTHELIAL** GROWTH CHARACTERISTICS OF YOLK SAC **STEM** CELLS

DETDESC:

DETD(105)

These . . . blood forming cells. As individual blood islands develop, their endothelial outer layers fuse with neighboring blood islands, forming a rudimentary **vascular** network, and the inner cells of the blood island mature to become the functional blood cells of the early embryo.

DETDESC:

DETD(128)

Tissues . . . optimal isolation period was approximately 4-6 weeks. At this time, a well defined yolk sac was present but an extensive **vascular** network had not yet formed, i.e., blood cells had not yet begun to migrate into the embryo in a prominent. . .

CLAIMS:

CLMS(17)

17. A method of producing **endothelial** cells in vitro, comprising culturing, in the presence of a growth factor, a substantially homogeneous population of murine yolk sac **stem** cells displaying a phenotype of CD34.sup.-, MHC class I.sup.- and MHC class II.sup.- which are capable of forming tubular structures.

CLAIMS:

CLMS(35)

35. A method of producing **endothelial** cells in vitro, comprising culturing, in the presence of a growth factor, a substantially homogeneous population of human yolk sac **stem** cells displaying a phenotype of CD34.sup.-, MHC class I.sup.- and MHC class II.sup.- which are capable of forming tubular structures.

US PAT NO: 5,681,714 [IMAGE AVAILABLE] L6: 6 of 16

SUMMARY:

BSUM(6)

Angiogenesis in both the embryo and adult requires the differentiation, proliferation, and migration of endothelial cells. Tissue transplantation studies with quail/chick chimeras have established that the developmental cues for both endothelial cell differentiation and proper patterning of **vessels** are extracellular and not pre-programmed within the cell (Noden, D. M. (1988) Development, 103, 121-140) Several peptide hormones, such as. . .

SUMMARY:

BSUM(10)

In particular, the present inventors using reverse transcription coupled to the polymerase chain reaction (RT-PCR) **isolated** from murine embryonic heart a cDNA, designated tek, whose deduced amino acid sequence corresponds to a novel RTK. The tek. . . present inventors have also shown by in situ hybridization that tek is expressed in the endocardium as well as the **endothelial** lining of the **vasculature**. tek was also found to be expressed in both mature **endothelial** cells and their **progenitors**, suggesting that the signalling pathways regulated by tek may be important to both the determination and proliferation of cells of the **endothelial** lineage. The tek locus of humans was mapped to the human chromosome 9p21 region. This region is deleted or rearranged. . .

SUMMARY:

BSUM(12)

The . . . polypeptide specifically detected by antibody directed against the novel receptor tyrosine kinase protein in both cultured endothelial cells and highly **vascularized** embryonic tissues. A 140-kDa protein was also specifically precipitated from cells transfected with the cDNA.

SUMMARY:

BSUM(13)

The present inventors have further elucidated the role of the novel receptor tyrosine kinase within the **endothelial** cell lineage by disrupting its signalling pathway using two different genetic approaches. First, transgenic mice expressing a dominant-negative form of. . . tyrosine kinase protein were constructed. Second, a null allele of the tek locus was created by homologous recombination in embryonic **stem** cells. Transgenic mice expressing dominant-negative alleles of tek or homozygous for the null allele of the tek locus both died. . . the tek gene confirmed that the tek signalling pathway plays a critical role in the differentiation, proliferation and survival of **endothelial** cells in the mouse embryo.

SUMMARY:

BSUM(26)

The . . . the novel receptor tyrosine kinase of the invention in tissues and cells. The antibodies may therefore be used to monitor **angiogenesis**, cardiogenesis and tumorigenesis.

SUMMARY:

BSUM(33)

The . . . the present invention. The methods of the invention will also be useful for identifying substances which may affect cardiogenesis and **angiogenesis** and/or maintenance of cells of the endothelial lineage and which may play a role in tumorigenesis.

SUMMARY:

BSUM(34)

Substances which affect **angiogenesis**, cardiogenesis or tumorigenesis

may be identified using the methods of the invention by comparing the pattern and level of expression. . .

DRAWING DESC:

DRWD(14)

FIG. 6E is a photograph showing expression of von Willebrand factor in the endothelial lining of the blood **vessels** of the maternal decidua;

DRAWING DESC:

DRWD(15)

FIG. 6F is a photograph showing expression of von Willebrand factor in the endothelial lining of the blood **vessels** in the cephalic region:

DRAWING DESC:

DRWD(16)

FIG. 6G is a photograph showing expression of von Willebrand factor in the endothelial lining of the blood **vessel** in the saggital section;

DRAWING DESC:

DRWD(18)

FIG. 6I is a photograph showing expression of von Willebrand factor in the endothelial lining of the blood **vessels** of the heart region;

DRAWING DESC:

DRWD(29)

FIG. 9A is a photograph showing the expression of a nucleic acid molecule of the invention in adult **vasculature** and in particular bright field illumination of a section through the upper heart region of a 3 week-old mouse hybridized. . .

DRAWING DESC:

DRWD(61)

FIG. 23A is a photograph showing tek-promoter-lacZ expression in the yolk sac **vasculature** of [normal and tek.sup..DELTA.sp homozygous embryos as follows: 23A shows expression in] Day 8.5 normal embryos;

DRAWING DESC:

DRWD(62)

FIG. 23B is a photograph showing tek-promoter-lacZ expression in the yolk sac **vasculature** of Day 9.0 normal embryos;

DRAWING DESC:

DRWD(63)

FIG. 23C is a photograph showing tek-promoter-lacZ expression in the yolk sac **vasculature** of Day 8.5 homozygous mutants;

DRAWING DESC:

DRWD(64)

FIG. 23D is a photograph showing tek-promoter-lacZ expression in the yolk sac **vasculature** of Day 9.0 homozygous mutants;

DRAWING DESC:

DRWD(80)

It . . . tyrosine kinase protein extracellular domain likely also plays a role in guiding the proper patterning of endothelial cells during blood **vessel** formation, both in the embryo and in the adult.

DRAWING DESC:

DRWD(84)

The . . . protein which comigrates with the polypeptide specifically detected by Tek antibody in both cultured endothelial cells (Py 4-1) and highly **vascularized** embryonic tissues (heart and umbilical vein). The Tek receptor tyrosine kinase protein cytoplasmic domain expressed in E. coli was shown. . .

DRAWING DESC:

DRWD(95)

In . . . layers, one mesodermal and the other ectodermal in origin. This membrane shares several features with the endothelial lining of blood **vessels**, such as having an epithelial-like morphology and the requirement to contain fluid within an enclosed cavity. Thus, this tissue may. . .

DRAWING DESC:

DRWD(96)

Specifically, . . . well as sectioned and whole mount embryos, showed that tek is specifically expressed in the endocardium, the leptomeninges and the **endothelial** lining of the **vasculature** from the earliest stages of their development. Moreover, examination of the morphology of tek-expressing cells, and staging of tek expression relative to that of the **endothelial** cell marker von Willebrand factor, revealed that tek is expressed prior to von Willebrand factor and appears to mark the embryonic **progenitors** of mature **endothelial** cells. Thus, tek encodes a novel putative receptor tyrosine kinase that may be critically involved in the determination and/or maintenance of cells of the **endothelial** lineage.

DRAWING DESC:

DRWD(97)

Overall, . . . 100, 339-349; Coffin, J. D. & Poole, T. J. (1988). Development, 102, 735-748). Thus, it is likely that orchestration of **vascularization** in the two vertebrate species is very similar. Studies on cell lineage relations carried out primarily in the chick (Noden,. . . migrate from mesoderm and populate the embryo with precursor cells that eventually contribute to the formation of the intraembryonic blood **vessels**.

DRAWING DESC:

DRWD(100)

The present inventors' work suggested that tek is expressed in the

presumptive precursors of **endothelial** cells, the angioblasts. First, tek expression was detected in both von Willebrand factor-positive cells as well as cells that appear to be **progenitors** of **endothelial** cells. Second, tek expression was observed in cells of non-**endothelial** morphology that in the avian system have been identified previously as angioblasts. It may also be significant that in the. . . (1989), Mol. Cell. Med., 6, 263-274 who showed in mouse tissue transplantation studies that lacZ-expressing somite tissue, while devoid of **endothelial** cells prior to transplantation, possess cells capable of migrating and contributing to the host **vasculature**. Taken together, the present inventors' work suggests that tek expression may constitute one of the earliest mammalian **endothelial** cell lineage markers described to date.

DRAWING DESC:

DRWD(102)

Tek expression is very low in adults. However, it is likely that expression will be upregulated upon induction of **angiogenesis**. Accordingly, tek likely plays a role in **angiogenesis**, for example in tumor growth, in mature animals in addition to its role during development.

DRAWING DESC:

DRWD(125)

Within . . . of Tek protein. Such antibodies will be useful in the diagnosis and treatment of developmental disorders of endothelial cell growth, **angiogenesis**, **vascularization**, wound healing and tumorigenesis.

DRAWING DESC:

DRWD(137)

As . . . expression patterns found for the novel tyrosine kinase of the invention indicate that it plays unique and important roles in **angiogenesis**, cardiogenesis and tumorigenesis. Therefore, the above described methods for detecting nucleic acid molecules and fragments thereof and Tek protein and parts thereof, can be used to monitor **angiogenesis**, cardiogenesis and tumorigenesis by detecting and localizing the novel tyrosine kinase protein of the invention.

DRAWING DESC:

DRWD(138)

It . . . to study the developmental expression of Tek and, accordingly, will provide further insight into the role of Tek protein in **angiogenesis**, cardiogenesis and tumorigenesis.

DRAWING DESC:

DRWD(139)

The . . . is only expressed in cells of the endothelial lineage permits the identification of substances such as ligands, which may affect **angiogenesis** and/or maintenance of cells of the endothelial lineage and which may play a role in tumorigenesis. Therefore, in accordance with. . .

DRAWING DESC:

DRWD(151)

The . . . form a ligand/receptor complex and activating tyrosine kinase activity thereby affecting signalling pathways, particularly those involved in the regulation of **angiogenesis**.

DRAWING DESC:

DRWD(156)

The . . . protein of the present invention. The methods of the invention are therefore useful for identifying potential stimulators or inhibitors of **angiogenesis**, cardiogenesis or tumorigenesis.

DRAWING DESC:

DRWD(161)

The invention further provides a method for assaying for a substance that affects **angiogenesis**, cardiogenesis, or tumorigenesis comprising administering to a non-human animal or to a tissue of an animal, a substance suspected of affecting **angiogenesis**, cardiogenesis, or tumorigenesis and detecting, and optionally quantitating, the novel receptor tyrosine kinase of the invention in the non-human animal. . .

DRAWING DESC:

DRWD(163)

Substances . . . banding of ligands and Tek protein, identified by the methods of the invention, may be used for stimulating or inhibiting **angiogenesis** or cardiogenesis, or inhibiting tumorigenesis. The efficacy of these substances in the treatment of human conditions may be confirmed using. . .

DRAWING DESC:

DRWD(165)

Null alleles may be generated in cells, such as embryonic **stem** cells by a deletion mutation. A recombinant Tek gene may also be engineered to contain an insertion mutation which inactivates Tek. Such a construct may then be introduced into a cell, such as an embryonic **stem** cell, by a technique such as transfection, electroporation, injection etc. Cell lacking an intact Tek gene may then be identified,. . . by assaying for expression of Tek protein using the methods described herein. Such cells may then be fused to embryonic **stem** cells to generate transgenic non-human animals deficient in Tek. Germline transmission of the mutation may be achieved, for example, by aggregating the embryonic **stem** cells with early stage embryos, such as 8 cell embryos, in vitro; transferring the resulting blastocysts into recipient females and;. . . aggregation chimeras. Such a mutant animal may be used to define specific nerve cell populations, developmental patterns of cardiogenesis, and **endothelial** and highly **vascularized** tissue and in vivo processes, normally dependent on Tek expression.

DETDESC:

DETD(43)

FIG. . . . readily detected in the heart, the leptomeninges lining the brain and spinal cord, and the inner lining of major blood **vessels**, including the caudal vein and basilar and renal arteries. In addition, thin bands of hybridization are observed in the intersomite regions, corresponding to tek expression in the intersegmental

vessels. Close examination of the region of the developing heart (FIG. 5B and 5C) reveals that tek is expressed in the. . . VI aortic arches, the sinus venosus, and the sino-auricular septum. In addition, tek expression is observed in numerous small blood **vessels** perforating the liver and mandible. These observations, together with the overall pattern of hybridization seen in the 12.5 day embryo, demonstrate that tek is expressed in the endothelial cells of the tunica interna, the innermost lining of the blood **vessels**; hence the designation tunica interna endothelial cell kinase, tek.

DETDESC:

DETD(44)

More . . . 6.5 and 7 day embryos revealed that while tek is expressed strongly in the inner lining of the small blood **vessels** and capillaries of the maternal decidua, no expression is observed in either the embryo itself or the ectoplacental cone. The. . .

DETDESC:

DETD(45)

FIG. . . . Adjacent section to A at higher magnification showing expression of von Willebrand factor in the endothelial lining of the blood **vessels** of the maternal decidua. Bar: 200 .mu.m. F. High magnification of cephalic region in A showing silver grains over a. . .

DETDESC:

DETD(46)

RNA . . . In addition, sagittal sections reveal numerous focal areas of hybridization throughout the cephalic mesenchyme in regions thought to contain developing **vasculature**, as well as a small number of tek-expressing cells extending beneath the ventral surface of the somites (FIG. 6H and. . .

DETDESC:

DETD(47)

Whole . . . II, III, first, second and third aortic arches; DA. dorsal aorta; E, endocardium; G, foregut pocket; H, heart; IS, intersegmental **vessel**; My, myocardium;; NF, neural fold; OT; otic vesicle; V, vitelline vein; Y, yolk sac. Bars: 250 .mu.m.

DETDESC:

DETD(48)

Consistent . . . be expressed in these same areas, and in the paired dorsal aortae, the vitelline veins, and in the forming intersegmental **vessels** (FIG. 7). By this time, tek expression was clearly confined to blood **vessels** within the embryo. On Day 9, tek expression was seen in addition, in the aortic arches and expression was very. . .

DETDESC:

DETD(50)
Expression of tek in **endothelial** cell **progenitors**

DETDESC:

DETD(51)

The observation that tek is expressed between Day 8.0 and 8.5 in focal regions thought to represent developing blood **vessels** raised the possibility that tek might be expressed in **endothelial** cell **progenitors**. Indeed, close inspection of hybridized sections from 8 to 8.5 day embryos revealed that while the expression the tek in the maternal decidua is restricted to cells of an **endothelial** cell morphology, tek expressing cells in the embryo are of two morphologically distinct cell types. In the developing blood islands. . . of the yolk sac, where tek expression is first detected, silver grains are localized predominantly to elongated cells with characteristic **endothelial** cell morphology (FIG. 6C). In contrast, within the cephalic mesenchyme, silver grains are frequently observed over large, round cells that,. . . during arian embryogenesis (Pardanaud et al., 1987; Coffin & Poole, 1988; Noden, 1989; Noden, 1991), correspond to angioblasts, the presumptive **progenitor** of **endothelial** cells (FIG. 6F). Both cell types are observed in the developing endocardium (FIG. 6I) which, at later stages, is known to contain only fully mature **endothelial** cells.

DETDESC:

DETD(52)

To . . . the maternal decidua and the embryo at Day 8.5, expression of von Willebrand factor is observed only in the tek-expressing, **vascular** endothelial cells of the maternal decidua (FIG. 6D and 6E). Hence tek expression precedes that of von Willebrand factor during embryogenesis. The same scenario is observed at later developmental stages during **vascularization** of individual organs.

DETDESC:

DETD(53)

FIG. . . . developing leptomeninges; A. Absence of immunohistochemical staining of von Willebrand factor in Day 12.5 leptomeninges. Arrow denotes a large blood **vessel** faintly positive for von Willebrand factor. B. In situ detection of tek expression in Day 12.5 leptomeninges. C. Staining of. . .

DETDESC:

DETD(54)

FIG. . . . factor, these observations, together with those on the morphology of tek-expressing cells, suggest that tek is expressed in both mature **endothelial** cells and their **progenitors**.

DETDESC:

DETD(56)
tek is expressed in adult **vasculature**

DETDESC:

DETD(57)

While the above results establish that tek is expressed during **vascularization** of the embryo, it was also of interest to determine whether expression of tek is maintained in endothelial cells of. . . week-old mouse revealed that tek is expressed in the endocardium as well as in the endothelial lining of major blood **vessels**, both arteries and veins, connecting with the adult heart (FIG. 9).

DETDESC:

DETD(58)

FIG. 9 shows the expression of tek in adult **vasculature**. A. Bright field illumination of a section through the upper heart region of a 3 week-old mouse hybridized with an. . .

DETDESC:

DETD(60)

The intensity of the hybridization signal observed for these structures is considerably lower than that observed for the endocardium and blood **vessels** of 12.5 day embryos hybridized and processed in parallel. This could indicate that mature endothelial cells, which are thought to. . .

DETDESC:

DETD(97)

FIG. . . . documented for endothelial cell populations cultured from different anatomical sites (Gerritsen, Biochem. Pharmacol., 36, 2701-2711, 1987 Gumkowski et al., Blood **Vessels**, 24, 11-23, 1987), the differential retention of expression of these markers following malignant transformation or in vitro culture, or the. . .

DETDESC:

DETD(129)

Interestingly, one of the embryos isolated on E9.5 had an enlarged pericardial cavity and contained few blood cells in the **vessels** of the yolk sac. This was likely due to hemorrhaging into the yolk sac cavity, as primitive red blood cells. . .

DETDESC:

DETD(132)

No . . . argues that the observed phenotypes for both the tek- and polyoma-promoter driven transgenes were intrinsic to a defect in the **vascular** endothelium.

DETDESC:

DETD(149)

FIGS. . . . Stained thin sections through the yolk sac of tek.sup..DELTA.sp heterozygous (22C) and homozygous (22F) embryos showing the distended yolk sac **vessels** and the decreased number of endothelial cells lining the yolk sac **vessels** (arrowheads). Bars: 30 .mu.m.

DETDESC:

DETD(150)

FIG. 23A-D shows the yolk sac **vasculature** of tek.sup..DELTA.sp homozygous embryos contain fewer endothelial cells. tek-promoter-lacZ transgene expression in Day 8.5 normal (23A) and tek.sup..DELTA.sp homozygous (23C). . .

DETDESC:

DETD(151)

FIGS. 24A-D shows the embryonic **vasculature** of tek.sup..DELTA.sp homozygous embryos contain fewer endothelial cells. The trunk (24A, 24C) and heart (24B, 24D) regions of a E9.0. . . homozygous (24A, 24B) and wild type (24C, 24D) embryos. A lower levels of lacZ expression is seen in the intersegmental **vessels** (is) and endocardium (e) of mutants. Dorsal aorta, da. Bars: 50 .mu.m.

DETDESC:

DETD(153)

The histological analysis of the yolk sacs from wild-type or heterozygous embryos harvested on E9.5 revealed that the blood **vessels** in the yolk sac appeared distended (FIGS. 23C & D) and were very often packed with blood (FIG. 24C &. . . however, blood could be detected in the yolk sac cavity, indicating that the lack of blood in the yolk sac **vasculature** was due to hemorrhaging. In addition, the yolk sac **vessels** contained considerably fewer endothelial cells (FIG. 22F) than heterozygous littermates (FIG. 22C). Furthermore, **vascular** hemorrhaging of homozygous embryos could also be detected histologically when the trunk region was examined. Primitive blood cells could be. . . 22B & E). The dorsal aorta in heterozygous embryos was well defined with endothelial cells lining the lumen of the **vessel** and there was no blood in the trunk (FIG. 22B). In contrast, in homozygous embryos the endothelium of the dorsal. . . disorganized and appeared to have ruptured, resulting in blood cells in the body (FIG. 22E). Localized hemorrhaging of the embryonic **vasculature** most likely results in a decrease in the embryonic blood pressure which may explain the accumulation of blood in the yolk sac **vasculature** and embryonic portion of the placenta (FIG. 22D). This region of the placenta also had very few endothelial cells in. . .

DETDESC:

DETD(156)

That . . . with a flk-1 antisense riboprobe. Both heterozygous and homozygous embryos (data not shown) contained flk-1-positive cells organized in a distinctive **vascular** network. However, the flk-1 positive cells in homozygous mutant embryos were present in discontinuous chains, suggesting that the **vessels** contained a sparsely populated endothelium (data not shown). Moreover the levels of flk-1 expression were lower in the homozygous mutants.. . .

DETDESC:

DETD(159)

Based on .beta.-galactosidase (.beta.-gal) activity, tek.sup..DELTA.sp homozygous embryos isolated on E8.5 and E9.0 contained a normally patterned **vasculature** in both extra- and embryonic tissues (FIGS. 24A-D and data not shown). Moreover, the size of normal and homozygous embryos. . . (FIGS. 24A-D and 25A-D, and data not shown). Histological examination of E9.0 homozygous embryos confirmed that proper patterning of the **vasculature** was initiated (FIGS. 24A & B, and data not shown). Furthermore, the endocardium and other **vascular** structures of mutant embryos formed correctly but contained only low levels of LacZ expression, in keeping with the low levels. . .

DETDESC:

DETD(160)

FIGS. . . . the levels of .beta.-Galactosidase activity in the mutants. In addition, increased blood cell number can be seen in the blood **vessels** of tek.sup..DELTA.sp homozygous embryos. Bars: A&C=25 .mu.m; B&D=12.5 .mu.m.

US PAT NO: 5,660,825 [IMAGE AVAILABLE] L6: 7 of 16

ABSTRACT:
A . . . of the C5b-9 complex. The compositions can be used in vitro to inhibit C5b-9 related stimulatory responses of platelets and **vascular** endothelium of perfused organs and tissues, thereby preventing the C5b-9 initiated cell necrosis or stimulated secretion of proteolytic enzymes and. . .

SUMMARY:

BSUM(5)

Recently, the C5b-9 proteins of the human plasma complement system have been implicated in non-lytic stimulatory responses from certain human **vascular** and blood cells. The capacity of C5b-9 to modify membrane permeability and to selectively alter ion conductance is thought to elicit these non-lytic responses from human cells. In the case of human blood platelets and **vascular** endothelium, assembly of the C5b-9 complex initiates a transient and reversible depolarization of the plasma membrane potential, a rise in. . .

SUMMARY:

BSUM(7)

This . . . and coagulation systems at the surface of blood platelets and endothelium can generate inflammatory and chemotactic peptides at sites of **vascular** thrombus formation and may contribute to the altered hemostasis associated with immune disease states. In addition, immune reactions affecting blood. . . and vasoactive amines from platelet storage granules, and increase adherence of platelets and leukocytes to the endothelial lining of blood **vessels**.

SUMMARY:

BSUM(9)

In . . . also adversely affected by the spontaneous activation of the complement system, resulting in membrane insertion of the C5b-9 proteins into **vascular** endothelium. Activation of C5 to C5 a and C5b has been shown to be catalyzed by plastics and other synthetic membranes required to maintain perfusion of **vascular** beds during in vitro tissue and organ storage. In addition, membrane deposition of C5b-9 in vivo has been implicated in. . .

SUMMARY:

BSUM(10)

Platelet . . . the subendothelium, which is known to occur in regions of atheromatous degeneration and suggests localized generation of C5a at the **vessel** wall, is potentially catalyzed by adherent platelets and b) local intravascular complement activation resulting in membrane deposition of C5b-9 complexes accompanies coronary **vessel** occlusion and may affect the ultimate extent of myocardial damage associated with infarction.

SUMMARY:

BSUM(17)

The compositions can be used in vitro to inhibit C5b-9 related stimulatory responses of platelets and **vascular** endothelium of perfused organs and tissues, thereby preventing the C5b-9 initiated cell necrosis or stimulated secretion of proteolytic enzymes and. . . the exposure of the procoagulant membrane receptors during collection and in vitro storage. In one variation of this embodiment, the **vascular** endothelium of organs and tissues to be transplanted are treated with these compositions to protect these cells from complement activation. . .

DETDESC:

DETD(2)

37 . . . the studies detailed below indicate that a deletion or inactivation of these cell surface components would increase the risk of **vascular** thrombosis and lead to a decreased storage time for platelets and platelet rich plasma (PRP), and perfused organs and transplanted. . .

DETDESC:

DETD(69)

In this context, it is important to note that affected red cells obtained from patients with the acquired **stem** cell disorder Paroxysmal Nocturnal Hemoglobinuria (PNH) have been shown to exhibit abnormal sensitivity to lysis by the C5b-9 proteins. This. . . of complement mediated disorders, particularly in view of the discovery that the inhibitor is also found on the surface of **endothelial** cells. As a result, administration of the inhibitor protein, whether **purified** from cells or expressed from cells engineered using recombinant techniques, or portions of the peptide having the same measurable activity,. . .

DETDESC:

DETD(70)

Treatment . . . immune disorders and diseases such as immunovasculitis, rheumatoid arthritis, scleroderma, disseminated intravascular coagulation, lupus, paroxysmal nocturnal hemoglobinuria, thrombotic thrombolytic purpura, **vascular** occlusion, reocclusion after surgery, coronary thrombosis, and myocardial infarction, is accomplished by administering an effective amount of a composition containing. . .

DETDESC:

DETD(73)

In . . . organs and tissue for transplantation, the C5b-9 inactivators would be added to the perfusate or storage medium to protect the **vascular** lining cells from ongoing complement activation during in vitro storage. Additionally, by coating these endothelial cells with a membrane-anchored C5b-9. . .

CLAIMS:

CLMS(2)

2. . . . disease selected from the group consisting of disseminated intravascular coagulation, lupus, rheumatoid arthritis, scleroderma,

paroxysmal nocturnal hemoglobinuria, thrombotic thrombolytic purpura, **vascular** occlusion, reocclusion, coronary thrombosis, myocardial infaction, and complement mediated inflammatory **vascular** disorders.

CLAIMS:

CLMS(6)

6. The method of claim 2 whereto the disorder is a complement mediated inflammatory **vascular** disorder.

US PAT NO: 5,635,178 [IMAGE AVAILABLE] L6: 8 of 16

SUMMARY:

BSUM(5)

Recently, the C5b-9 proteins of the human plasma complement system have been implicated in non-lytic stimulatory responses from certain human **vascular** and blood cells. The capacity of C5b-9 to modify membrane permeability and to selectively alter ion conductance is thought to elicit these non-lytic responses from human cells. In the case of human blood platelets and **vascular** endothelium, assembly of the C5b-9 complex initiates a transient and reversible depolarization of the plasma membrane potential, a rise in. . .

SUMMARY:

BSUM(7)

This . . . and coagulation systems at the surface of blood platelets and endothelium can generate inflammatory and chemotactic peptides at sites of **vascular** thrombus formation and may contribute to the altered hemostasis associated with immune disease states. In addition, immune reactions affecting blood. . . and vasoactive amines from platelet storage granules, and increase adherence of platelets and leukocytes to the endothelial lining of blood **vessels**.

SUMMARY:

BSUM(9)

In . . . also adversely affected by the spontaneous activation of the complement system, resulting in membrane insertion of the C5b-9 proteins into **vascular** endothelium. Activation of C5 to C5a and C5b has been shown to be catalyzed by plastics and other synthetic membranes required to maintain perfusion of **vascular** beds during in vitro tissue and organ storage. In addition, membrane deposition of C5b-9 in vivo has been implicated in. . .

SUMMARY:

BSUM(10)

Platelet . . . the subendothelium, which is known to occur in regions of atheromatous degeneration and suggests localized generation of C5a at the **vessel** wall, is potentially catalyzed by adherent platelets and b) local intravascular complement activation resulting in membrane deposition of C5b-9 complexes accompanies coronary **vessel** occlusion and may affect the ultimate extent of myocardial damage associated with infarction.

SUMMARY:

BSUM(17)

The compositions can be used in vitro to inhibit C5b-9 related stimulatory responses of platelets and **vascular** endothelium of perfused organs and tissues, thereby preventing the C5b-9 initiated cell necrosis or stimulated secretion of proteolytic enzymes and. . . the exposure of the procoagulant membrane receptors during collection and in vitro storage. In one variation of this embodiment, the **vascular** endothelium of organs and tissues to be transplanted are treated with these compositions to protect these cells from complement activation. . .

DETDESC:

DETD(2)

37 . . . the studies detailed below indicate that a deletion or inactivation of these cell surface components would increase the risk of **vascular** thrombosis and lead to a decreased storage time for platelets and platelet rich plasma (PRP), and perfused organs and transplanted. . .

DETDESC:

DETD(69)

In this context, it is important to note that affected red cells obtained from patients with the acquired **stem** cell disorder Paroxysmal Nocturnal Hemoglobinuria (PNH) have been shown to exhibit abnormal sensitivity to lysis by the C5b-9 proteins. This. . . of complement mediated disorders, particularly in view of the discovery that the inhibitor is also found on the surface of **endothelial** cells. As a result, administration of the inhibitor protein, whether **purified** from cells or expressed from cells engineered using recombinant techniques, or portions of the peptide having the same measurable activity,. . .

DETDESC:

DETD(70)

Treatment . . . immune disorders and diseases such as immunovasculitis, rheumatoid arthritis, scleroderma, disseminated intravascular coagulation, lupus, paroxysmal nocturnal hemoglobinuria, thrombotic thrombolytic purpura, **vascular** occlusion, reocclusion after surgery, coronary thrombosis, and myccardial infarction, is accomplished by administering an effective amount of a composition containing. . .

DETDESC:

DETD(73)

In . . . organs and tissue for transplantation, the C5b-9 inactivators would be added to the perfusate or storage medium to protect the **vascular** lining cells from ongoing complement activation during in vitro storage. Additionally, by coating these endothelial cells with a membrane-anchored C5b-9. . .

CLAIMS:

CLMS(2)

2. . . . disease selected from the group consisting of disseminated intravascular coagulation, lupus, rheumatoid arthritis, scleroderma, paroxysmal nocturnal hemoglobinuria, thrombotic thrombolytic purpura,

vascular occlusion, reocclusion, coronary thrombosis, myocardial infarction, and complement mediated inflammatory **vascular** disorders.

US PAT NO: 5,635,156 [IMAGE AVAILABLE] L6: 9 of 16

SUMMARY:

BSUM(51)

The hematopoietic microenvironment plays a major role in the engraftment of hematopoietic **stem** cells. In addition to being a source of growth factors and cellular interactions for the survival and renewal of **stem** cells, it may also provide physical space for these cells to reside. A number of cell types collectively referred to as stromal cells are found in the vicinity of the hematopoietic **stem** cells in the bone marrow microenvironment. These cells include both bone marrow-derived CD45.sup.+ cells and non-bone marrow-derived CD45.sup.- cells, such as adventitial cells, reticular cells, **endothelial** cells and adipocytes.

DETDESC:

DETD(21)

The . . . of hematopoietic cells and stromal cells. The stromal cells occupy much space of the bone marrow environment and they include **endothelial** cells that line the sinusoids, fibroblastic cells such as adventitial reticular cells, perisinusoidal adventitial cells, periarterial adventitial cells, intersinusoidal reticular. . . Rev. Immunol. 8: 111; Greenberger, 1991, Crit. Rev. Oncology/Hematology 11: 65). In addition, the Applicant has recently identified, characterized and **purified** a previously unknown cell type from the bone marrow that facilitates the engraftment of bone marrow **stem** cells across allogeneic and xenogeneic barriers. This cell referred to as hematopoietic facilitatory cell must be matched with the **stem** cell at the MHC for it to enhance **stem** cell engraftment. The facilitatory cells express a unique profile of cell surface markers: Thy-1.sup.+, CD3.sup.+, CD8.sup.+, CD45.sup.+ CD45R.sup.+, MHC class. . .

DETDESC:

DETD(22)

The various stromal cell types express a number of well-characterized surface markers, including but not limited to, **vascular** addressing, mannosyl and galactosyl residues, fasciculin III, villin, tetrapeptide, neural cell adhesion molecule receptor, hemonectin, B1 integrins, B2 integrins and. . .

US PAT NO: 5,599,703 [IMAGE AVAILABLE] L6: 10 of 16

ABSTRACT:
The present invention relates to a method of amplifying in vitro stemcells. In this method hematopoietic CD34.sup.+ **stem** and **progenitor** cells are **isolated** from human bone marrow and contacted with **endothelial** cells. The contacted **stem** cells and **endothelial** cells are cultured in the presence of at least one cytokine in an amount sufficient to support amplification/expansion of the hematopoietic CD34.sup.+ **stem** and **progenitor** cells. This method produces increased yields of hematopoietic CD34.sup.+ **stem** and **progenitor** cells which can be used in human therapeutics.

SUMMARY:

BSUM(3)

The present invention relates to a method of amplifying/expanding hematopoietic **stem** cells. In particular, the present invention relates to the amplification/expansion of human bone marrow **stem** cells by culturing cells with **endothelial** cells in the presence of growth factors or cytokines.

SUMMARY:

BSUM(5)

Hematopoiesis, . . . involves a complex scheme of multilineage differentiation (Metcalf, Nature 339:27-30, 1989). Hematopoiesis occurs mainly in the bone marrow where hematopoietic **stem** cells (pluripotential **stem** cells) proliferate and differentiate into **progenitor** cells which then develop into different types of mature blood cells (Gordon et al., Bone Marrow Transplant 4:335, 1989; Dexter et al., Ann. Rev. Cell Bio. 3:423, 1987). The hematopoietic **stem** and **progenitor** cell is functionally characterized by its extensive and prolonged self-renewal capacity as well as its ability to differentiate and thereby. . . et al., J. Immunol. 133:157, 1984; Strauss et al., Exp. Hematol. 14:878, 1986). Phenotypically, the only well defined human hematopoietic **stem** and **progenitor** cell marker at present is the CD34 hematopoietic cell surface antigen (Civin et al., J. Immunol. 133:157, 1984; Strauss et. . . J. Exp. Med. 172:355, 1990; Berstein et al., Blood 77:2316, 1991). In addition, the CD34 antigen is expressed on human **vascular endothelial** cells (Fina et al., Blood 75:2417, 1990), suggesting a possible role for the antigen in adhesion or cellular interactions. **Purified** CD34.sup.+ **stem** and **progenitor** cells can reconstitute hematopoiesis in vivo (Berenson et al., J. Clin. Invest. 81:951, 1988; Berenson, et al., Blood 77:1717, 1991). . . J. Haematol. 60:129, 1985; Verfaillie et al, J. Exp. Med. 172:509, 1990). Additional studies have demonstrated that the pluripotent hematopoietic **stem** cell can be identified by additional phenotypic markers, singly and in combination. The most primitive pluripotent human bone marrow hematopoietic **stem** cells are small (low forward light scatter and side scatter) CD34.sup.+, Thy1.sup.+/-, c-kit.sup.+, HLA-DR.sup.-, CD38.sup.-, CD15.sup.-, rhodamine-123 dull and 4-hydroperoxycyclophosphamide-resistant. . . Craig et al, J Exp Med 177:1331, 1993). Similarly, recent purification experiments have shown that the most primitive murine hematopoietic **stem** cells have been **isolated** with the use of a variety of phenotypic markers, such as Thy-1, c-kit, wheat-germ agglutinin (WGA), and **stem** cell antigen (Okada et al, Blood 78:1706, 1991; Ikuta and Weissman, Proc Natl Acad Sci USA 89:1502, 1992) but are. . .

SUMMARY:

BSUM(6)

The bone marrow serves in vivo as the requisite microenvironment where constitutive hematopoiesis, **stem** cell differentiation and **stem** cell self-renewal occurs (Gordon et al., Bone Marrow Transplant 4:335, 1989; Dexter et al., Ann. Rev. Cell Bio. 3:423, 1987;. . . microenvironment has two major components--the lymphohematopoietic elements and the bone marrow stroma. The bone marrow stroma, made up of fibroblasts, **endothelial** cells, adipocytes and macrophages/monocytes, provides a heterogeneous adherent cell layer. Only these heterogeneous adherent cell layers have been shown to be effective in supporting long-term in vitro CD34.sup.+ **stem** and **progenitor** cell proliferation and differentiation (Dorshkind, Annu. Rev. Immunol. 8:111, 1990; Dexter et al., J. Cell Physiol. 91:335, 1977; Allan et al., Exp. Hematol. 12:517, 1984). Within the bone marrow stroma, CD34.sup.+ hematopoietic **stem** and **progenitor** cells undergo self-renewal, proliferation and differentiation (Andrews et al., J. Exp. Med. 172:355, 1990; Sutherland et al., Blood 74:1563, 1989;. . . et al., J. Cell

Physiol. 130:150,1987; Gordon et al., Br. J. Haematol. 60:129, 1985). The proliferation and differentiation of CD34.sup.+ **stem** and **progenitor** cell in stromal dependent cultures is thought to involve cell-to-cell interactions (Andrews et al., J. Exp. Med. 172:355, 1990; Verfaillie. . .

SUMMARY:

BSUM(8)

Hematopoietic . . . systems can be broadly classified into two groups, liquid culture and stromal coculture systems. Liquid culture systems grow CD34.sup.+ hematopoietic **stem** and **progenitor** cells suspended in liquid media with additional growth factors and cytokines (Haylock et al, Blood 80: 1405, 1992; Brugger et. . . 1993). Although liquid cultures are easy to maintain and are technically well suited for large scale expansion of CD34.sup.+ hematopoietic **stem** and **progenitor** cells for use in therapy, they have uniformly been unsuccessful in generating expanded numbers of CD34.sup.+ **stem** and **progenitor** cells that are necessary for long term engraftment. This is also reflected in the fact that it is difficult to maintain these cultures over a long period of time (months) as the CD34.sup.+ **stem** cells all quickly differentiate into more mature cells. The inability to maintain and expand a proliferating pool of undifferentiated CD34.sup.+ **stem** and **progenitor** cells is thought to be due to the lack of the appropriate microenvironment generated by the bone marrow stromal elements. To rectify this problem, stromal coculture systems grow CD34.sup.+ hematopoietic **stem** and **progenitor** cells on or within an adherent layer of bone marrow stroma (a heterogeneous population of **endothelial** cells, adipocytes, fibroblasts and macrophages), with or without the addition of growth factors and cytokines.

SUMMARY:

BSUM(24)

To . . . and broadly described herein, the invention in one embodiment comprises a method of amplifying/expanding in vitro human bone marrow CD34.sup.+ **stem** and **progenitor** cells. The method comprises **isolating** CD34.sup.+ **stem** cells from human bone marrow; contacting the **isolated stem** and **progenitor** cells with **endothelial** cells; and culturing the **stem** and **progenitor** and **endothelial** cells in the presence of at least one cytokine in an amount sufficient to support amplification/expansion of the CD34.sup.+ **stem** and **progenitor** cells.

SUMMARY:

BSUM(25)

In another embodiment, the present invention comprises a method of engrafting CD34.sup.+ **stem** and **progenitor** cells in a patient. In this CD34.sup.+ **stem** and **progenitor** cells are first **isolated** from human bone marrow. Then, the CD34.sup.+ **stem** and **progenitor** cells are contacted with **endothelial** cells and the combination is cultured in the presence of at least one cytokine in an amount sufficient to support amplification/expansion of the CD34.sup.+ **stem** and **progenitor** cells. After amplification/expansion, the CD34.sup.+ **stem** and **progenitor** cells are **isolated** from the culture and infused into the patient.

SUMMARY:

BSUM(26)

In . . . patient to allow for the rapid, short term reconstitution of mature blood cells in the circulation. In this method CD34.sup.+ **stem** and **progenitor** cells are first **isolated** from human bone marrow. Then, the CD34.sup.+ **stem** and **progenitor** cells are contacted with **endothelial** cells and the combination is cultured in the presence of at least one cytokine in an amount sufficient to support amplification/expansion and differentiation of the CD34.sup.+ bone marrow **stem** and **progenitor** cells. After amplification/expansion, the whole population of CD34.sup.+ **stem** and **progenitor** cells as well as more differentiated cells is infused into the patient.

DRAWING DESC:

DRWD(3)

FIG. 1 shows the effects of optimal concentrations of granulocyte-macrophage colony stimulating factor (GM-CSF)+**stem** cell factor (SCF), interleukin-3 (IL-3)+SCF+interleukin-6 (IL-6), and GM-CSF+IL-3+SCF+IL-6 on the production of nonadherent cells in liquid suspension cultures (n=6), noncontact porcine brain microvascular **endothelial** cells (PMVEC) cultures (n=6), and contact PMVEC cultures (n=12). Each column represents the mean number of total viable nonadherent cells.+-.1SD harvested after 7 days of culture per 1.times.10.sup.5 human CD34.sup.+ bone marrow **stem** and **progenitor** cells initially cultured. Results from five different experiments are depicted.

DETDESC:

DETD(2)

The . . . relates to an in vitro culture system that supports the proliferation and amplification/expansion of both primitive hematopoietic bone marrow blood **stem** cells (CD34.sup.+ CD38.sup.-) and CD34.sup.+ **progenitor** cells for all hematopoietic cell lineages. Using **endothelial** cells treated with cytokines, a culture system was developed which supports primitive hematopoietic **stem** cell amplification/expansion. In this culture system, **isolated** CD34.sup.+ **stem** and **progenitor** cells in contact with **endothelial** cells are cultured in the presence of cytokine(s) to promote the proliferation and amplification/expansion of the CD34.sup.+ **stem** and **progenitor** cells.

DETDESC:

DETD(5)

In the present culture system, the enriched CD34.sup.+ **stem** and **progenitor** cells are placed in direct contact with **endothelial** cells. Preferred **endothelial** cells are brain microvascular **endothelial** cells, more particularly, porcine brain microvascular **endothelial** cells (PMVEC). Examples of other **endothelial** cells suitable for use in the present invention include, but are not limited to, human **endothelial** cells, microvascular **endothelial** cells, brain **endothelial** cells, porcine **endothelial** cells and various types of immortalized **endothelial** cells.

DETDESC:

DETD(6)

It is important that the CD34.sup.+ **stem** and **progenitor** cells be in contact with the **endothelial** cells to maximize amplification/expansion. For example, the CD34.sup.+ **stem** and **progenitor** cells can be seeded onto a 70-100% semi-confluent

monolayer of PMVECs. Amplification/expansion of primitive hematopoietic CD34.sup.+ **stem** and **progenitor** cells in vitro increases significantly within 7 days when the CD34.sup.+ **stem** and **progenitor** cells are directly cultured on **endothelial** cells. This is in contrast to the result occurring when CD34.sup.+ **stem** and **progenitor** cells are cultured with **endothelial** cells in diffusion chambers preventing CD34.sup.+ **stem** cell-to-**endothelial** cell interactions.

DETDESC:

DETD(9)

CD34.sup.+ **stem** and **progenitor** cells are co-cultured with **endothelial** cells and are treated with cytokines in the present method. To promote amplification/expansion of the CD34.sup.+ **stem** and **progenitor** cells, cytokines matched to the species of CD34.sup.+ cells utilized are added to the CD34.sup.+ cell-**endothelial** cell culture. While use of at least a single cytokine is required for CD34.sup.+ cell amplification/expansion, combinations of cytokines can. . . be employed and are, in fact, preferred. Examples of suitable cytokine combinations for use in the amplification/expansion of human CD34.sup.+ **stem** and **progenitor** cells include, but are not limited to, GM-CSF alone; GM-CSF+SCF; IL-3+SCF+IL-6 and GM-CSF+IL-3+SCF+IL-6. Preferably, the CD34.sup.+ hematopoietic cell-**endothelial** cell culture is treated with GM-CSF+IL-3+SCF+IL-6. The amount of each cytokine used and the combination of cytokines selected will vary depending on several variables, but are readily determinable by those skilled in the art. For example, the CD34.sup.+ hematopoietic **stem** cells-**endothelial** cells can be cultured with 0.1-20.0 ng/ml of GM-CSF, 1.0-200.0 ng/ml of IL-3, 5.0-500.0 ng/ml of SCF and/or 1.0-100.0 ng/ml. . .

DETDESC:

DETD(10)

When highly **purified** CD34.sup.+ **stem** and **progenitor** cells were cultured with combinations of either GM-CSF+SCF, IL-3+SCF+IL-6 or GM-CSF+IL-3+SCF+IL-6 in liquid suspension for the short-term (7 days), no. . . in GM-CSF+IL-3+SCF+IL-6 treated cultures. These findings suggest that cytokines alone are not sufficient for the in vitro amplification/expansion of CD34.sup.+ **stem** and **progenitor** cells on **endothelial** monolayers and that CD34.sup.+ hematopoietic cell-to-PMVEC interactions, other soluble growth factors, membrane-bound growth factors, cellular adhesion molecules, or extracellular matrix proteins produced by cytokine activated **endothelial** cells may be involved. In addition, the **endothelial** cell-derived extracellular matrix may bind these growth factors and present these molecules in active form to the **stem** cell.

DETDESC:

DETD(13)

Accordingly, the present invention also relates to a method of engrafting CD34.sup.+ **stem** and **progenitor** cells in a patient. This method involves **isolation** of CD34.sup.+ **stem** and **progenitor** cells and co-culturing the **isolated** CD34.sup.+ **stem** and **progenitor** cells with **endothelial** cells in the presence of cytokines as discussed above. The method further requires the **isolation** of the amplified/expanded CD34.sup.+ **stem** cells from the culture. (The present method can also be used on unseparated bone marrow rather than **purified** CD34.sup.+ **stem** and **progenitor** cells.)

DETDESC:

DETD(48)

After various days of culture, non-adherent cells were gently removed from the **endothelial** cell monolayers, washed twice with complete culture medium, and manual hemacytometer cell counts were performed using trypan blue exclusion dye.. . . for each specific cytokine combination the fold increase in the harvested nonadherent cells was greatest in the cultures where CD34.sup.+ **stem** and **progenitor** cells were grown in contact with the PMVEC monolayer, intermediate in the transwell/noncontact culture and the least in the liquid. . .

CLAIMS:

CLMS(1)

What is claimed is:

1. A method of expanding human bone marrow CD34.sup.+ **stem** and **progenitor** cells, including primitive **stem** cells, in vitro comprising the steps of:

i) **isolating** the CD34.sup.+ **stem** and **progenitor** cells from human bone marrow;

ii) contacting the **isolated** CD34.sup.+ **stem** and **progenitor** cells with porcine microvascular brain **endothelial** cells; and

iii) co-culturing the contacted CD34.sup.+ **stem** and **progenitor** cells and **endothelial** cells in the presence of at least one cytokine in an amount sufficient to support amplification/expansion of said CD34+ **stem** and **progenitor** cells.

CLAIMS:

CLMS(2)

2. The method according to claim 1, wherein said CD34.sup.+ **stem** and **progenitor** cells are contacted with a semi-confluent monolayer of the **endothelial** cells.

CLAIMS:

CLMS(6)

6. A method of engrafting human bone marrow CD34.sup.+ **stem** and **progenitor** cells in a human in need of said CD34.sup.+ **stem** and **progenitor** cells, said method comprising the steps of:

i) **isolating** CD34.sup.+ **stem** and **progenitor** cells from human bone marrow;

ii) contacting the **isolated** CD34.sup.+ **stem** and **progenitor** cells with porcine microvascular brain **endothelial** cells containing a factor or factors that expand the CD34.sup.+ **stem** and **progenitor** cells;

iii) co-culturing the contacted CD34.sup.+ **stem** and **progenitor** cells and **endothelial** cells in the presence of at least one cytokine in an amount sufficient to support amplification/expansion of said CD34.sup.+ **stem** and **progenitor** cells;

iv) **isolating** the amplified/expanded CD34.sup.+ **stem** and **progenitor** cells from the culture; and

v) infusing the amplified/expanded CD34.sup.+ **stem** and **progenitor** cells into said human.

CLAIMS:

CLMS(9)

9. A method of amplifying/expanding human CD34.sup.+ bone marrow **stem** and **progenitor** cells in vitro which comprises the steps of:
i) **isolating** CD34.sup.+ **stem** and **progenitor** cells from human bone marrow;
ii) contacting the **isolated** CD34.sup.+ **stem** cells and **progenitor** cells with porcine microvascular brain **endothelial** cells; and
iii) co-culturing the contacted CD34.sup.+ **stem** cells and **progenitor** cells and **endothelial** cells in the presence of a mixture of granulocyte-macrophage colony stimulating factor, interleukin-3, **stem** cell factor and interleukin-6 in an amount sufficient to amplify/expand said CD34.sup.+ **stem** and **progenitor** cells.

US PAT NO: 5,573,940 [IMAGE AVAILABLE] L6: 11 of 16

SUMMARY:

BSUM(3)

Recently, the C5b-9 proteins of the human plasma complement system have been implicated in non-lytic stimulatory responses from certain human **vascular** and blood cells. The capacity of C5b-9 to modify membrane permeability and to selectively alter ion conductance is thought to elicit these non-lytic responses from human cells. In the case of human blood platelets and **vascular** endothelium, assembly of the C5b-9 complex initiates a transient and reversible depolarization of the plasma membrane potential, a rise in. . .

SUMMARY:

BSUM(5)

This . . . and coagulation systems at the surface of blood platelets and endothelium can generate inflammatory and chemotactic peptides at sites of **vascular** thrombus formation and may contribute to the altered hemostasis associated with immune disease states. In addition, immune reactions affecting blood. . . and vasoactive amines from platelet storage granules, and increase adherence of platelets and leukocytes to the endothelial lining of blood **vessels**.

SUMMARY:

BSUM(7)

In . . . also adversely affected by the spontaneous activation of the complement system, resulting in membrane insertion of the C5b-9 proteins into **vascular** endothelium. Activation of C5 to C5a and C5b has been shown to be catalyzed by plastics and other synthetic membranes required to maintain perfusion of **vascular** beds during in vitro tissue and organ storage. In addition, membrane deposition of C5b-9 in vivo has been implicated in. . .

SUMMARY:

BSUM(8)

Assembly . . . C4b2a and C3bBb (C5-convertases). The activity of these two enzymes is normally inhibited on the surface of human blood and **vascular** membranes by the plasma membrane proteins, "membrane cofactor protein" (CD46), described by Lublin and Atkinson, Current Topics Microbiol. Immunol. 153:123. . .

SUMMARY:

BSUM(9)

Platelet . . . the subendothelium, which is known to occur in regions of atheromatous degeneration and suggests localized generation of C5a at the **vessel** wall, is potentially catalyzed by adherent platelets and b) local intravascular complement activation resulting in membrane deposition of C5b-9 complexes accompanies coronary **vessel** occlusion and may affect the ultimate extent of myocardial damage associated with infarction.

SUMMARY:

BSUM(10)

There . . . now considerable evidence that the human erythrocyte membrane as well as the plasma membranes of other human blood cells and **vascular endothelium** are normally protected from these effects of complement by cell-surface proteins that specifically inhibit activation of the C5b-9 pore upon. . . by a glycolipid anchor, and are deleted from the membranes of the most hemolytically sensitive erythrocytes that arise in the **stem** cell disorder paroxysmal nocturnal hemoglobinuria; (2) the activity of both inhibitors is species-restricted, showing selectivity for C8 and C9 that. . .

SUMMARY:

BSUM(11)

In . . . of the C5b-9 complex. The compositions can be used in vitro to inhibit C5b-9 related stimulatory responses of platelets and **vascular** endothelium of perfused organs and tissues, thereby preventing the C5b-9 initiated cell necrosis or stimulated secretion of proteolytic enzymes and. . . the exposure of the procoagulant membrane receptors during collection and in vitro storage. In one variation of this embodiment, the **vascular** endothelium of organs and tissues to be transplanted are treated with these compositions to protect these cells from complement activation. . .

SUMMARY:

BSUM(17)

A . . . with a vector containing the gene at 12 to 24 hours prior to infusion or transplantation. In the case of **vascularized** organs to be transplanted, transfection of the recombinant gene of the **vascular** endothelial cells lining the blood **vessels** is performed.

DETDESC:

DETD(3)

The . . . and the studies detailed below indicate that a deletion or inactivation of these cell surface components increases the risk of **vascular** thrombosis and leads to a decreased storage time for platelets and platelet rich plasma (PRP), and perfused organs and transplanted. . .

DETDESC:

DETD(72)

Platelets obtained from patients with the acquired **stem** cell disorder Paroxysmal Nocturnal Hemoglobinuria (PNH) have been shown to exhibit abnormal sensitivity to fluid phase complement activation, as

characterized. . . . of complement mediated disorders, particularly in view of the discovery that the inhibitor is also found on the surface of **endothelial** cells. As a result, administration of the inhibitor protein, whether **purified** from cells or expressed from cells engineered using recombinant techniques, or portions of the peptide having the same measurable activity,. . .

DETDESC:

DETD(73)

Treatment . . . immune disorders and diseases such as immunovasculitis, rheumatoid arthritis, scleroderma, disseminated intravascular coagulation, lupus, paroxysmal nocturnal hemoglobinuria, thrombotic thrombolytic purpura, **vascular** occlusion, reocclusion after surgery, coronary thrombosis, and myocardial infarction, is accomplished by administering an effective amount of a composition containing. . .

DETDESC:

DETD(75)

In . . . organs and tissue for transplantation, the C5b-9 inactivators would be added to the perfusate or storage medium to protect the **vascular** lining cells from ongoing complement activation during in vitro storage. Additionally, by coating these endothelial cells with a membrane-anchored C5b-9. . . the technique of transfection or infection at 12 to 24 hours prior to infusion or transplantation. In the case of **vascularized** organs to be transplanted, transfection of the plasmid of the **vascular** endothelial cells lining the blood **vessels** is performed. It may be preferable in some cases to transfect the gene encoding CD59 of the same species as. . .

US PAT NO: 5,559,022 [IMAGE AVAILABLE] L6: 12 of 16

SUMMARY:

BSUM(6)

The . . . liver is the parenchymal cells (PC), also known as hepatocytes. The liver also contains several other cell types such as **endothelial** cells, adipocytes, fibroblastic cells and Kupffer cells, collectively referred to as stromal (littoral) cells. The ability of liver cells to. . . regeneration, when the liver is damaged or partially removed, has led to speculation for the existence of a population of **stem** cells or reserve cells, capable of self-renewal and differentiation. However, prior to the present invention, such liver reserve cells had. . .

SUMMARY:

BSUM(7)

"Oval" . . . mammalian liver. These cells have a high nuclear to cytoplasmic size ratio, are approximately 40% of the diameter of freshly **isolated** PC, express enzyme activities consistent with those of fetal hepatocytes, and have a relatively high proliferation rate (Tsao et al.,. . . PC retrodifferentiation (Grisham, 1980, Ann. N.Y. Acad. Sci. 349:128-137; Firminger, 1955, J. Nat. Cancer Instit. 15:1427-1441) but they may resemble **endothelial** cells more closely (Fausto et al., 1987, In: Cell Separation: Methods and selected applications, Vol. 4, T. G. Pretlow II and T. P. Pretlow, editors, Academic Press, London, pp 45-78). The role of oval cells as putative **stem** cells or reserve cells has never been established, and it has been the subject of a number

of investigations (Fausto. . .

SUMMARY:

BSUM(14)

The . . . U.S. Pat. No. 5,032,508). The stromal compartment contains all of the adherent cells found in liver tissues including Kupffer cells, **vascular** and bile duct endothelial cells, fibroblasts, and some adipocyte-like cells. These cells elaborate a matrix similar in some respects to. . .

US PAT NO: 5,550,108 [IMAGE AVAILABLE] L6: 13 of 16

ABSTRACT:
A . . . of the C5b-9 complex. The compositions can be used in vitro to inhibit C5b-9 related stimulatory responses of platelets and **vascular** endothelium of perfused organs and tissues, thereby preventing the C5b-9 initiated cell necrosis or stimulated secretion of proteolytic enzymes and. . .

SUMMARY:

BSUM(5)

Recently, the C5b-9 proteins of the human plasma complement system have been implicated in non-lytic stimulatory responses from certain human **vascular** and blood cells. The capacity of C5b-9 to modify membrane permeability and to selectively alter ion conductance is thought to elicit these non-lytic responses from human cells. In the case of human blood platelets and **vascular** endothelium, assembly of the C5b-9 complex initiates a transient and reversible depolarization of the plasma membrane potential, a rise in. . .

SUMMARY:

BSUM(7)

This . . . and coagulation systems at the surface of blood platelets and endothelium can generate inflammatory and chemotactic peptides at sites of **vascular** thrombus formation and may contribute to the altered hemostasis associated with immune disease states. In addition, immune reactions affecting blood. . . and vasoactive amines from platelet storage granules, and increase adherence of platelets and leukocytes to the endothelial lining of blood **vessels**.

SUMMARY:

BSUM(9)

In . . . also adversely affected by the spontaneous activation of the complement system, resulting in membrane insertion of the C5b-9 proteins into **vascular** endothelium. Activation of C5 to C5a and C5b has been shown to be catalyzed by plastics and other synthetic membranes required to maintain perfusion of **vascular** beds during in vitro tissue and organ storage. In addition, membrane deposition of C5b-9 in vivo has been implicated in. . .

SUMMARY:

BSUM(10)

Platelet . . . the subendothelium, which is known to occur in regions of atheromatous degeneration and suggests localized generation of C5a at the **vessel** wall, is potentially catalyzed by adherent platelets and

b) local intravascular complement activation resulting in membrane deposition of C5b-9 complexes accompanies coronary **vessel** occlusion and may affect the ultimate extent of myocardial damage associated with infarction.

SUMMARY:

BSUM(17)

The compositions can be used in vitro to inhibit C5b-9 related stimulatory responses of platelets and **vascular** endothelium of perfused organs and tissues, thereby preventing the C5b-9 initiated cell necrosis or stimulated secretion of proteolytic enzymes and. . . the exposure of the procoagulant membrane receptors during collection and in vitro storage. In one variation of this embodiment, the **vascular** endothelium of organs and tissues to be transplanted are treated with these compositions to protect these cells from complement activation. . .

DETDESC:

DETD(2)

37 . . . the studies detailed below indicate that a deletion or inactivation of these cell surface components would increase the risk of **vascular** thrombosis and lead to a decreased storage time for platelets and platelet rich plasma (PRP), and perfused organs and transplanted. . .

DETDESC:

DETD(69)

In this context, it is important to note that affected red cells obtained from patients with the acquired **stem** cell disorder Paroxysmal Nocturnal Hemoglobinuria (PNH) have been shown to exhibit abnormal sensitivity to lysis by the C5b-9 proteins. This. . . of complement mediated disorders, particularly in view of the discovery that the inhibitor is also found on the surface of **endothelial** cells. As a result, administration of the inhibitor protein, whether **purified** from cells or expressed from cells engineered using recombinant techniques, or portions of the peptide having the same measurable activity,. . .

DETDESC:

DETD(70)

Treatment . . . immune disorders and diseases such as immunovasculitis, rheumatoid arthritis, scleroderma, disseminated intravascular coagulation, lupus, paroxysmal nocturnal hemoglobinuria, thrombotic thrombolytic purpura, **vascular** occlusion, reocclusion after surgery, coronary thrombosis, and myocardial infarction, is accomplished by administering an effective amount of a composition containing. . .

DETDESC:

DETD(73)

In . . . organs and tissue for transplantation, the C5b-9 inactivators would be added to the perfusate or storage medium to protect the **vascular** lining cells from ongoing complement activation during in vitro storage. Additionally, by coating these endothelial cells with a membrane-anchored C5b-9. . .

US PAT NO: 5,514,364 [IMAGE AVAILABLE] L6: 14 of 16

SUMMARY:

BSUM(49)

The hematopoietic microenvironment plays a major role in the engraftment of hematopoietic **stem** cells. In addition to being a source of growth factors and cellular interactions for the survival and renewal of **stem** cells, it may also provide physical space for these cells to reside. A number of cell types collectively referred to as stromal cells are found in the vicinity of the hematopoietic **stem** cells in the bone marrow microenvironment. These cells include both bone marrow-derived CD45.sup.+ cells and non-bone marrow-derived CD45.sup.- cells, such as adventitial cells, reticular cells, **endothelial** cells and adipocytes.

DETDESC:

DETD(19)

The . . . of hematopoietic cells and stromal cells. The stromal cells occupy much space of the bone marrow environment and they include **endothelial** cells that line the sinusoids, fibroblastic cells such as adventitial reticular cells, perisinusoidal adventitial cells, periarterial adventitial cells, intersinusoidal reticular. . . 1990, Annu. Rev. Immunol. 8:111; Greenberger, 1991, Crit. Rev. Oncology/Hematology 11:65). In addition, the Applicant has recently identified, characterized and **purified** a previously unknown cell type from the bone marrow that facilitates the engraftment of bone marrow **stem** cells across allogeneic and xenogeneic barriers. This cell referred to as hematopoietic facilitatory cell must be matched with the **stem** cell at the MHC for it to enhance **stem** cell engraftment. The facilitatory cells express a unique profile of cell surface markers: Thy-1.sup.+, CD3.sup.+, CD8.sup.+, CD45.sup.+ CD45R.sup.+, MHC class. . .

DETDESC:

DETD(20)

The various stromal cell types express a number of well-characterized surface markers, including but not limited to, **vascular** addressing, mannosyl and galactosyl residues, fasciculin III, villin, tetrapeptide, neural cell adhesion molecule receptor, hemonectin, B1 integrins, B2 integrins and. . .

US PAT NO: 5,409,710 [IMAGE AVAILABLE] L6: 15 of 16

DETDESC:

DETD(2)

One method for forming a foam cell involves contacting an **isolated** foam cell precursor with a foam cell stimulating ligand. In vivo, foam cells typically arise from circulating monocytes that have become deposited beneath the **vascular endothelium**, although the derivation of foam cells from smooth-muscle cells has also been reported. (Steinberg, D., et al., NEJM 320(14):915-923 (1989). Thus, in vitro, the preferred foam cell precursors include **isolated stem** cells and **stem** cell derivatives, such as monocytes and macrophages, as well as smooth muscle cells. **Isolated stem** cells are prepared according to U.S. Pat. Nos. 5,004,681 and 5,061,620, the contents of which patents are incorporated herein by reference. **Stem** cell derivatives are prepared by contacting the **isolated stem** cells with

differentiation agents under conditions known to induce differentiation of the **stem** cell to the desired cell type. For example, contacting a monocyte with macrophage-colony stimulating factor (M-CSF) results in differentiation of. . .

DETDESC:

DETD(91)

Macrophages . . . The cells are optionally co-incubated in the presence of a lipoprotein containing agent, or are subsequently transferred to a culture **vessel** containing a lipoprotein containing agent. Preferably, the **vessel** contains an excess concentration of lipoprotein-containing agent, e.g., at least about a 5-fold excess and preferably, at least about a. . .

US PAT NO: 5,135,916 [IMAGE AVAILABLE] L6: 16 of 16

SUMMARY:

BSUM(5)

Recently, the C5b-9 proteins of the human plasma complement system have been implicated in non-lytic stimulatory responses from certain human **vascular** and blood cells. The capacity of C5b-9 to modify membrane permeability and to selectively alter ion conductance is thought to elicit these non-lytic responses from human cells. In the case of human blood platelets and **vascular** endothelium, assembly of the C5b-9 complex initiates a transient and reversible depolarization of the plasma membrane potential, a rise in. . .

SUMMARY:

BSUM(7)

This . . . and coagulation systems at the surface of blood platelets and endothelium can generate inflammatory and chemotactic peptides at sites of **vascular** thrombus formation and may contribute to the altered hemostasis associated with immune disease states. In addition, immune reactions affecting blood. . . and vasoactive amines from platelet storage granules, and increase adherence of platelets and leukocytes to the endothelial lining of blood **vessels**.

SUMMARY:

BSUM(9)

In . . . also adversely affected by the spontaneous activation of the complement system, resulting in membrane insertion of the C5b-9 proteins into **vascular** endothelium. Activation of C5 to C5a and C5b has been shown to be catalyzed by plastics and other synthetic membranes required to maintain perfusion of **vascular** beds during in vitro tissue and organ storage. In addition, membrane deposition of C5b-9 in vivo has been implicated in. . .

SUMMARY:

BSUM(10)

Platelet . . . the subendothelium, which is known to occur in regions of atheromatous degeneration and suggests localized generation of C5a at the **vessel** wall, is potentially catalyzed by adherent platelets and b) local intravascular complement activation resulting in membrane deposition of C5b-9 complexes accompanies coronary **vessel** occlusion and may affect the ultimate extent of myocardial damage associated with

infarction.

SUMMARY:

BSUM(17)

The compositions can be used in vitro to inhibit C5b-9 related stimulatory responses of platelets and **vascular** endothelium of perfused organs and tissues, thereby preventing the C5b-9 initiated cell necrosis or stimulated secretion of proteolytic enzymes and. . . the exposure of the procoagulant membrane receptors during collection and in vitro storage. In one variation of this embodiment, the **vascular** endothelium of organs and tissues to be transplanted are treated with these compositions to protect these cells from complement activation. . .

DETDESC:

DETD(2)

37 . . . the studies detailed below indicate that a deletion or inactivation of these cell surface components would increase the risk of **vascular** thrombosis and lead to a decreased storage time for platelets and platelet rich plasma (PRP), and perfused organs and transplanted. . .

DETDESC:

DETD(68)

In this context, it is important to note that affected red cells obtained from patients with the acquired **stem** cell disorder Paroxysmal Nocturnal Hemoglobinuria (PNH) have been shown to exhibit abnormal sensitivity to lysis by the C5b-9 proteins. This. . . of complement mediated disorders, particularly in view of the discovery that the inhibitor is also found on the surface of **endothelial** cells. As a result, administration of the inhibitor protein, whether **purified** from cells or expressed from cells engineered using recombinant techniques, or portions of the peptide having the same measurable activity,. . .

DETDESC:

DETD(69)

Treatment . . . immune disorders and diseases such as immunovasculitis, rheumatoid arthritis, scleroderma, disseminated intravascular coagulation, lupus, paroxysmal nocturnal hemoglobinuria, thrombotic thrombolytic purpura, **vascular** occlusion, reocclusion after surgery, coronary thrombosis, and myocardial infarction, is accomplished by administering an effective amount of a composition containing. . .

DETDESC:

DETD(72)

In . . . organs and tissue for transplantation, the C5b-9 inactivators would be added to the perfusate or storage medium to protect the **vascular** lining cells from ongoing complement activation during in vitro storage. Additionally, by coating these endothelial cells with a membrane-anchored C5b-9. . .

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* * * * * * * * * * * * * * * * * * * * * * * * *
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  *       APS is unavailable Thanksgiving Day, Christmas Day,       *
  *       and New Year's Day.                                       *
  *                                                                 *
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FILE 'USPAT' ENTERED AT 10:16:53 ON 08 NOV 1998

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  *               W E L C O M E   T O   T H E                     *
  *          U. S.   P A T E N T   T E X T   F I L E              *
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=> e isner/in

E#	FILE	FREQUENCY		TERM
E1	USPAT	1		ISNARDI, MICHAEL ANTHONY/IN
E2	USPAT	2		ISNARDON, GERALD/IN
E3	USPAT	0	-->	ISNER/IN
E4	USPAT	1		ISNER, ANDREW B/IN
E5	USPAT	8		ISNER, JEFFREY M/IN
E6	USPAT	3		ISNER, ROBERT E/IN
E7	USPAT	1		ISNER, WILLIAM G/IN
E8	USPAT	1		ISO AHO, KALEVI/IN
E9	USPAT	1		ISO, AKIO/IN
E10	USPAT	1		ISO, BASARIC/IN
E11	USPAT	1		ISO, HARUO/IN
E12	USPAT	1		ISO, KAZUSHIGE/IN

=> s e5

L1 8 "ISNER, JEFFREY M"/IN

=> d l1 1-8

1. 5,830,879, Nov. 3, 1998, Treatment of vascular injury using vascular endothelial growth factor; **Jeffrey M. Isner**, 514/44; 435/69.4, 69.6, 69.8, 91.2, 320.1; 536/23.5, 23.51 [IMAGE AVAILABLE]

2. 5,652,225, Jul. 29, 1997, Methods and products for nucleic acid delivery; **Jeffrey M. Isner**, 514/44; 424/93.2; 435/320.1; 536/23.5, 23.51; 604/51, 52, 53 [IMAGE AVAILABLE]

3. 5,368,034, Nov. 29, 1994, Method and apparatus for thrombolytic therapy; **Jeffrey M. Isner**, 600/439, 455, 504 [IMAGE AVAILABLE]

4. 5,106,386, Apr. 21, 1992, Catheter; **Jeffrey M. Isner**, et al., 606/15 [IMAGE AVAILABLE]

5. 5,104,393, Apr. 14, 1992, Catheter; **Jeffrey M. Isner**, et al., 606/15 [IMAGE AVAILABLE]

6. 4,997,431, Mar. 5, 1991, Catheter; **Jeffrey M. Isner**, et al., 606/15 [IMAGE AVAILABLE]

7. 4,985,028, Jan. 15, 1991, Catheter; **Jeffrey M. Isner**, et al., 606/15 [IMAGE AVAILABLE]

8. 4,862,886, Sep. 5, 1989, Laser angioplasty; Richard H. Clarke, et al., 606/7; 372/53, 57, 70, 108; 385/33; 606/15, 17 [IMAGE AVAILABLE]

=> s l1 and (endothel?)(P)(progenitor? or stem)

```
          7150 ENDOTHEL?
          1778 PROGENITOR?
         87797 STEM
           268 (ENDOTHEL?)(P)(PROGENITOR? OR STEM)
L2           0 L1 AND (ENDOTHEL?)(P)(PROGENITOR? OR STEM)
```

=> s (ischem? or angiogen? or vessel? or vascula?) and (endothel?)(P)(progenitor? or stem)

```
          6941 ISCHEM?
          1359 ANGIOGEN?
        193773 VESSEL?
         20754 VASCULA?
          7150 ENDOTHEL?
          1778 PROGENITOR?
         87797 STEM
           268 (ENDOTHEL?)(P)(PROGENITOR? OR STEM)
L3         174 (ISCHEM? OR ANGIOGEN? OR VESSEL? OR VASCULA?) AND (ENDOTHEL
?)(
               P)(PROGENITOR? OR STEM)
```

=> s (ischem? or angiogen? or vessel? or vascula?)(P)(endothel?)(P)(progenitor? or stem)

```
          6941 ISCHEM?
          1359 ANGIOGEN?
        193773 VESSEL?
         20754 VASCULA?
          7150 ENDOTHEL?
          1778 PROGENITOR?
         87797 STEM
L4          86 (ISCHEM? OR ANGIOGEN? OR VESSEL? OR VASCULA?)(P)(ENDOTHEL?)
(P)
               (PROGENITOR? OR STEM)
```

=> sl4(P)(treat? or therap? or administer?)

'SL4(P)(TREAT?' IS NOT A RECOGNIZED COMMAND

=> s l4(P)(treat? or therap? or administer?)

```
        564372 TREAT?
         83723 THERAP?
         90445 ADMINISTER?
L5          34 L4(P)(TREAT? OR THERAP? OR ADMINISTER?)
```

=> d l5 1-34

1. 5,830,644, Nov. 3, 1998, Method for screening for agents which increase telomerase activity in a cell; Michael D. West, et al., 435/6, 4, 7.2, 15, 91.2; 436/34, 63, 64, 94, 501 [IMAGE AVAILABLE]

2. 5,817,662, Oct. 6, 1998, Substituted amino alkyl compounds; J. Peter

Klein, et al., 514/263; 424/824, 825 [IMAGE AVAILABLE]

3. 5,807,862, Sep. 15, 1998, Therapeutic compounds containing pyrimidinyl moieties; J. Peter Klein, et al., 514/269; 544/309, 310, 311, 312 [IMAGE AVAILABLE]

4. 5,807,861, Sep. 15, 1998, Amine substituted xanthinyl compounds; J. Peter Klein, et al., 514/263 [IMAGE AVAILABLE]

5. 5,801,182, Sep. 1, 1998, Amine substituted compounds; J. Peter Klein, et al., 514/269, 274; 544/310, 311, 312 [IMAGE AVAILABLE]

6. 5,801,181, Sep. 1, 1998, Amino alcohol substituted cyclic compounds; John Michnick, et al., 514/263, 183, 249, 259, 274, 309, 315, 418, 425, 617, 619, 626, 668, 669 [IMAGE AVAILABLE]

7. 5,792,772, Aug. 11, 1998, Enatiomerically pure hydroxylated xanthine compounds; James A. Bianco, et al., 514/263 [IMAGE AVAILABLE]

8. 5,777,115, Jul. 7, 1998, Acetal-and ketal-substituted pyrimidine compounds; Alistair Leigh, et al., 544/242, 267 [IMAGE AVAILABLE]

9. 5,776,679, Jul. 7, 1998, Assays for the DNA component of human telomerase; Bryant Villeponteau, et al., 435/6, 91.2, 91.21, 91.51; 536/23.1, 24.31, 24.33 [IMAGE AVAILABLE]

10. 5,770,595, Jun. 23, 1998, Oxime substituted therapeutic compounds; J. Peter Klein, et al., 514/263; 544/271, 273 [IMAGE AVAILABLE]

11. 5,756,122, May 26, 1998, Liposomally encapsulated nucleic acids having high entrapment efficiencies, method of manufacturer and use thereof for transfection of targeted cells; Alain Thierry, et al., 424/450 [IMAGE AVAILABLE]

12. 5,750,396, May 12, 1998, Stable virus packaging cell lines; Yanping Yang, et al., 435/357, 320.1, 366; 536/23.72, 24.1 [IMAGE AVAILABLE]

13. 5,739,138, Apr. 14, 1998, Enantiomerically pure hydroxylated xanthine compounds to treat autoimmune diabetes; James A. Bianco, et al., 514/263, 866 [IMAGE AVAILABLE]

14. 5,707,624, Jan. 13, 1998, Treatment of Kaposi's sarcoma by inhibition of scatter factor; Brian J. Nickoloff, et al., 424/158.1, 143.1, 145.1, 152.1 [IMAGE AVAILABLE]

15. 5,695,932, Dec. 9, 1997, Telomerase activity assays for diagnosing pathogenic infections; Michael D. West, et al., 435/6, 91.1 [IMAGE AVAILABLE]

16. 5,670,506, Sep. 23, 1997, Halogen, isothiocyanate or azide substituted xanthines; Alistair Leigh, et al., 514/258, 263; 544/267, 272, 277 [IMAGE AVAILABLE]

17. 5,658,892, Aug. 19, 1997, Compound delivery using high-pressure impulse transients; Thomas J. Flotte, et al., 514/44; 204/155, 157.15; 536/22.1, 23.1; 607/72 [IMAGE AVAILABLE]

18. 5,652,243, Jul. 29, 1997, Methods of using enantiomerically pure hydroxylated xanthine compounds; James A. Bianco, et al., 514/263, 262, 265, 814 [IMAGE AVAILABLE]

19. 5,648,357, Jul. 15, 1997, Enatiomerically pure hydroxylated xanthine compounds; James A. Bianco, et al., 514/263, 267, 270, 271 [IMAGE AVAILABLE]

20. 5,645,986, Jul. 8, 1997, Therapy and diagnosis of conditions related to telomere length and/or telomerase activity; Michael D. West, et al., 435/6, 91.2, 183, 184, 194; 436/63; 536/24.31, 24.33 [IMAGE AVAILABLE]

21. 5,629,315, May 13, 1997, Treatment of diseases using enantiomerically pure hydroxylated xanthine compounds; James A. Bianco, et al., 514/263, 866 [IMAGE AVAILABLE]

22. 5,621,102, Apr. 15, 1997, Process for preparing enantiomerically pure xanthine derivatives; James A. Bianco, et al., 544/267 [IMAGE AVAILABLE]

23. 5,620,984, Apr. 15, 1997, Enatiomerically pure hydroxylated xanthine compounds to treat inflammatory diseases; James A. Bianco, et al., 514/263 [IMAGE AVAILABLE]

24. 5,612,349, Mar. 18, 1997, Enantiomerically pure hydroxylated xanthine compounds to treat shock symptoms; James A. Bianco, et al., 514/263, 921 [IMAGE AVAILABLE]

25. 5,583,016, Dec. 10, 1996, Mammalian telomerase; Bryant Villeponteau, et al., 435/91.3, 91.1, 91.31, 194, 252.3, 254.11, 320.1, 366, 369; 536/23.1, 23.2, 24.31, 24.33 [IMAGE AVAILABLE]

26. 5,580,874, Dec. 3, 1996, Enatiomerically pure hydroxylated xanthine compounds; James A. Bianco, et al., 514/263 [IMAGE AVAILABLE]

27. 5,580,873, Dec. 3, 1996, Enatiomerically pure hydroxylated xanthine compounds to treat proliferative vascular diseases; James A. Bianco, et al., 514/263 [IMAGE AVAILABLE]

28. 5,567,704, Oct. 22, 1996, R-enatiomerically pure hydroxylated xanthine compounds to treat baldness; James A. Bianco, et al., 514/263, 262 [IMAGE AVAILABLE]

29. 5,521,315, May 28, 1996, Olefin substituted long chain compounds; Gail Underiner, et al., 546/243; 544/285; 546/242 [IMAGE AVAILABLE]

30. 5,470,878, Nov. 28, 1995, Cell signaling inhibitors; John Michnick, et al., 514/558, 258, 262, 274, 299, 315, 418, 425, 529, 552, 561, 613, 617, 626, 629, 669; 544/254, 285, 301; 546/183, 243; 548/486, 556 [IMAGE AVAILABLE]

31. 5,440,041, Aug. 8, 1995, Acetal or ketal substituted xanthine compounds; Alistair Leigh, et al., 544/267, 268 [IMAGE AVAILABLE]

32. 5,428,070, Jun. 27, 1995, Treatment of vascular degenerative diseases by modulation of endogenous nitric oxide production of activity; John P. Cooke, et al., 514/557, 310 [IMAGE AVAILABLE]

33. 5,416,195, May 16, 1995, Polypeptide derivatives of granulocyte colony stimulating factor; Roger Camble, et al., 530/351; 424/85.1; 530/395; 930/145 [IMAGE AVAILABLE]

34. 5,354,756, Oct. 11, 1994, Olefin-substituted long chain xanthine compounds; Gail Underiner, et al., 514/263; 544/267, 272, 273 [IMAGE AVAILABLE]

=> d l5 1-34 kwic

US PAT NO: 5,830,644 [IMAGE AVAILABLE] L5: 1 of 34

SUMMARY:

BSUM(476)

Such activators of telomerase would be useful as **therapeutic** agents to forestall and reverse cellular senescence, including but not limited to conditions associated with cellular senescence, e.g., (a) cells with replicative capacity in the central nervous system, including astrocytes, **endothelial** cells, and fibroblasts which play a role in such age-related diseases as Alzheimer's disease, Parkinson's disease, Huntington's disease, and stroke,. . . capacity in the immune system such as B and T lymphocytes, monocytes, neutrophils, eosinophils, basophils, NK cells and their respective **progenitors**, which may play a role in age-related immune system impairment, (f) cells with a finite replicative capacity in the **vascular** system including **endothelial** cells, smooth muscle cells, and adventitial fibroblasts which may play a role in age-related diseases of the **vascular** system including atherosclerosis, calcification, thrombosis, and aneurysms, and (g) cells with a finite replicative capacity in the eye such as pigmented epithelium and **vascular endothelial** cells which may play an important role in age-related madular degeneration.

US PAT NO: 5,817,662 [IMAGE AVAILABLE] L5: 2 of 34

DETDESC:

DETD(45)

The . . . to growth factors capable of stimulating said proliferation and said amount is sufficient to inhibit said proliferation; (6) lower systemic **vascular** resistance conferred by **endothelial** cells and said amount is sufficient to reduce the release of hypertension-inducing substances; (7) lower systemic **vascular** resistance induced by **endothelial** cells and said amount is sufficient to enhance the release of anti-hypertensive substances; (8) lower expression of adhesion molecules induced. . . TNF, or endotoxin stimulated monocytes and macrophages; (13) prevent the release of platelet activating factor by IL-1, TNF, or endotoxin **treated** megakaryocytes, fibroblastic cells, and macrophages; (14) prevent the down-regulation of receptors for cytokines in TNF-**treated** hematopoietic **progenitor** cells and said amount is sufficient to prevent said down-regulation; (15) suppress the production of metalloproteases in IL-1-stimulated or TNF-stimulated. . .

US PAT NO: 5,807,862 [IMAGE AVAILABLE] L5: 3 of 34

DETDESC:

DETD(87)

The . . . the proliferation of smooth muscle cells in response to growth factors capable of stimulating said proliferation, being; (6) lower systemic **vascular** resistance conferred by **endothelial** cells, being; (7) lower systemic **vascular** resistance induced by **endothelial** cells, being; (8) lower expression of adhesion molecules induced by enhancers thereof, being; (9) suppress the activation of T-cells and. . . TNF, or endotoxin stimulated monocytes and macrophages; (13) prevent the release of platelet activating factor by IL-1, TNF, or endotoxin **treated** megakaryocytes, fibroblastic cells, and macrophages; (14) prevent the down-regulation of receptors for cytokines in TNF-**treated** hematopoietic **progenitor** cells, being; (15) suppress the production of metalloproteases in IL-1-stimulated or TNF-stimulated glomerular epithelial cells or synovial cells, being; (16). . .

US PAT NO: 5,807,861 [IMAGE AVAILABLE] L5: 4 of 34

DETDESC:

DETD(40)

The . . . (5) inhibit proliferation of smooth muscle cells in response to growth factors capable of stimulating said proliferation; (6) lower systemic **vascular** resistance conferred by **endothelial** cells by reducing release of hypertension-inducing substances; (7) lower systemic **vascular** resistance induced by **endothelial** cells by enhancing release of anti-hypertensive substances; (8) lower expression of adhesion molecules induced by enhancers thereof; (9) suppress activation. . . IL-1, TNF, or endotoxin stimulated monocytes and macrophages; (13) prevent release of platelet activating factor by IL-1, TNF, or endotoxin **treated** megakaryocytes, fibroblastic cells, and macrophages; (14) prevent down-regulation of receptors for cytokines in TNF-**treated** hematopoietic **progenitor** cells; (15) suppress production of metalloproteases in IL-1- or TNF-stimulated glomerular epithelial or synovial cells; (16) enhance resistance of gastrointestinal. . .

US PAT NO: 5,801,182 [IMAGE AVAILABLE] L5: 5 of 34

DETDESC:

DETD(40)

The . . . (5) inhibit proliferation of smooth muscle cells in response to growth factors capable of stimulating said proliferation; (6) lower systemic **vascular** resistance conferred by **endothelial** cells by reducing release of hypertension-inducing substances; (7) lower systemic **vascular** resistance induced by **endothelial** cells by enhancing release of anti-hypertensive substances; (8) lower expression of adhesion molecules induced by enhancers thereof; (9) suppress activation. . . IL-1, TNF, or endotoxin stimulated monocytes and macrophages; (13) prevent release of platelet activating factor by IL-1, TNF, or endotoxin **treated** megakaryocytes, fibroblastic cells, and macrophages; (14) prevent down-regulation of receptors for cytokines in TNF-**treated** hematopoietic **progenitor** cells; (15) suppress production of metalloproteases in IL-1- or TNF-stimulated glomerular epithelial or synovial cells; (16) enhance resistance of gastrointestinal. . .

US PAT NO: 5,801,181 [IMAGE AVAILABLE] L5: 6 of 34

DETDESC:

DETD(45)

The . . . to growth factors capable of stimulating said proliferation and said amount is sufficient to inhibit said proliferation; (6) lower systemic **vascular** resistance conferred by **endothelial** cells and said amount is sufficient to reduce the release of hypertension-inducing substances; (7) lower systemic **vascular** resistance induced by **endothelial** cells and said amount is sufficient to enhance the release of anti-hypertensive substances; (8) lower expression of adhesion molecules induced. . . TNF, or endotoxin stimulated monocytes and macrophages; (13) prevent the release of platelet activating factor by IL-1, TNF, or endotoxin **treated** megakaryocytes, fibroblastic cells, and macrophages; (14) prevent the down-regulation of receptors for cytokines in TNF-**treated** hematopoietic **progenitor** cells and said amount is sufficient to prevent said down-regulation; (15) suppress the production of metalloproteases in IL-1-stimulated or TNF-stimulated. . .

DETDESC:

DETD(85)

The . . . inhibit the proliferation of smooth muscle cells in response to growth factors capable of stimulating said proliferation; (6) lower systemic **vascular** resistance conferred by **endothelial** cells; (7) lower systemic **vascular** resistance induced by **endothelial** cells; (8) lower expression of adhesion molecules induced by enhancers thereof; (9) suppress the activation of T-cells and macrophages by. . . TNF, or endotoxin stimulated monocytes and macrophages; (13) prevent the release of platelet activating factor by IL-1, TNF, or endotoxin **treated** megakaryocytes, fibroblastic cells, and macrophages; (14) prevent the down-regulation of receptors for cytokines in TNF-**treated** hematopoietic **progenitor** cells; (15) suppress the production of metalloproteases in IL-1-stimulated or TNF-stimulated glomerular epithelial cells or synovial cells; (16) enhance the. . .

US PAT NO: 5,792,772 [IMAGE AVAILABLE] L5: 7 of 34

DETDESC:

DETD(62)

The . . . tumor cells and said amount is sufficient to inhibit said proliferation; or (2) a method to promote differentiation of hematopoietic **stem** cells into red blood cells, platelets, lymphocytes, and granulocytes, and said amount is sufficient to promote said proliferation; or (3). . . of stimulating said proliferation and said amount is sufficient to inhibit said proliferation; or (8) a method to lower systemic **vascular** resistance conferred by **endothelial** cells and said amount is sufficient to reduce the release of hypertension-inducing substances; or (9) a method to lower systemic **vascular** resistance induced by **endothelial** cells and said amount is sufficient to enhance the release of anti-hypertensive substances; or (10) a method to lower expression. . . is sufficient to enhance said resistance; or (14) a method to prevent the suppression of growth stimulatory factor production in TNF-**treated** bone marrow stromal cells and said amount is sufficient to prevent said suppression; or (I5) a method to prevent the. . . monocytes and macrophages; or (16) a method to prevent the release of platelet activating factor by IL-1, TNF, or endotoxin **treated** megakaryocytes, fibroblastic cells, and macrophages; or (17) a method to prevent the down-regulation of receptors for cytokines in TNF-**treated** hematopoietic **progenitor** cells and said amount is sufficient to prevent said down-regulation; or (18) a method to suppress the production of metalloproteases. . .

US PAT NO: 5,777,115 [IMAGE AVAILABLE] L5: 8 of 34

DETDESC:

DETD(81)

The . . . tumor cells and said amount is sufficient to inhibit said proliferation; or (2) a method to promote differentiation of hematopoietic **stem** cells into red blood cells, platelets, lymphocytes, and granulocytes, and said amount is sufficient to promote said proliferation; or (3). . . of stimulating said proliferation and said amount is sufficient to inhibit said proliferation; or (8) a method to lower systemic **vascular** resistance conferred by **endothelial** cells and said amount is sufficient to reduce the release of hypertension-inducing substances; or (9) a method to lower systemic **vascular** resistance induced by **endothelial** cells and said amount is sufficient to enhance the release of anti-hypertensive substances; or (10) a method to lower expression. . . is sufficient to enhance said

resistance; or (14) a method to prevent the suppression of growth stimulatory factor production in TNF-**treated** bone marrow stromal cells and said amount is sufficient to prevent said suppression; or (15) a method to prevent the. . . monocytes and macrophages; or (16) a method to prevent the release of platelet activating factor by IL-1, TNF, or endotoxin **treated** megakaryocytes, fibroblastic cells, and macrophages; or (17) a method to prevent the down-regulation of receptors for cytokines in TNF-**treated** hematopoietic **progenitor** cells and said amount is sufficient to prevent said down-regulation; or (18) a method to suppress the production of metalloproteases. . .

US PAT NO: 5,776,679 [IMAGE AVAILABLE] L5: 9 of 34

DETDESC:

DETD(40)

Cells that can be targeted for telomerase gene **therapy** (**therapy** involving increasing the telomerase activity of a target cell) include but are not limited to hematopoietic **stem** cells (AIDS and post-chemotherapy), **vascular endothelial** cells (cardiac and cerebral **vascular** disease), skin fibroblasts and basal skin keratinocytes (wound healing and burns), chondrocytes (arthritis), brain astrocytes and microglial cells (Alzheimer's Disease),. . .

US PAT NO: 5,770,595 [IMAGE AVAILABLE] L5: 10 of 34

DETDESC:

DETD(78)

The . . . of tumor cells and said amount is sufficient to inhibit said proliferation; or a method to promote differentiation of hematopoietic **stem** cells into red blood cells, platelets, lymphocytes, and granulocytes, and said amount is sufficient to promote said proliferation; or (3). . . of stimulating said proliferation and said amount is sufficient to inhibit said proliferation; or (8) a method to lower systemic **vascular** resistance conferred by **endothelial** cells and said amount is sufficient to reduce the release of hypertension-inducing substances; or (9) a method to lower systemic **vascular** resistance induced by **endothelial** cells and said amount is sufficient to enhance the release of anti-hypertensive substances; or (10) a method to lower expression. . . is sufficient to enhance said resistance; or (14) a method to prevent the suppression of growth stimulatory factor production in TNF-**treated** bone marrow stromal cells and said amount is sufficient to prevent said suppression; or (15) a method to prevent the. . . monocytes and macrophages; or (16) a method to prevent the release of platelet activating factor by IL-1, TNF, or endotoxin **treated** megakaryocytes, fibroblastic cells, and macrophages; or (17) a method to prevent the down-regulation of receptors for cytokines in TNF-**treated** hematopoietic **progenitor** cells and said amount is sufficient to prevent said down-regulation; or (18) a method to suppress the production of metalloproteases. . .

US PAT NO: 5,756,122 [IMAGE AVAILABLE] L5: 11 of 34

SUMMARY:

BSUM(26)

In accordance with another aspect of the invention there is provided a liposome prepared by the methods described above, wherein the **therapeutic** protein is selected from the group consisting of platelet-derived growth factor, epidermal growth factor, interleukins 1-14, granulocyte colony stimulating factor, granulocyte-macrophage

colony stimulating factor, tumor necrosis factor, leukemia inhibitory factor, amphiregulin, **angiogenin**, betacellulin, calcitonin, ciliary neurotrophic factor, brain-derived neurotrophic factor, neurotrophins 3 and 4, nerve growth factor, colony stimulating factor-1, **endothelial** cell growth factor, erythropoietin, acidic and basic fibroblast growth factor, hepatocyte growth factor, heparin binding EGF-like growth factor, insulin, insulin-like. . . and II, interferons .alpha., .beta., and .gamma., keratinocyte growth factor, macrophage inflammatory protein .alpha. and .beta., midkine, oncostatin M, RANTES, **stem** cell factor, transforming growth factors .alpha. and .beta., and **vascular endothelial** growth factor.

CLAIMS:

CLMS(17)

17. A liposome according to claim 15, wherein said **therapeutic** protein is selected from the group consisting of platelet-derived growth factor, epidermal growth factor, interleukins 1-14, granulocyte colony stimulating factor, granulocyte-macrophage colony stimulating factor, tumor necrosis factor, leukemia inhibitory factor, amphiregulin, **angiogenin**, betacellulin, calcitonin, ciliary neurotrophic factor, brain-derived neurotrophic factor, neurotrophins 3 and 4, nerve growth factor, colony stimulating factor-1, **endothelial** cell growth factor, erythropoietin, acidic and basic fibroblast growth factor, hepatocyte growth factor, heparin binding EGF-like growth factor, insulin, insulin-like. . . II, interferons .alpha., .beta., and .gamma., keratinocyte growth factor, macrophage inflammatory protein .alpha. .beta., and .gamma. midkine, oncostatin M, RANTES, **stem** cell factor, transforming growth factors .alpha. and .beta., and **vascular endothelial** growth factor.

US PAT NO: 5,750,396 [IMAGE AVAILABLE] L5: 12 of 34

SUMMARY:

BSUM(5)

The . . . to transfer exogenous genes into human somatic cells and achieve expression of the transferred gene at levels that are of **therapeutic** value would create many opportunities for human gene **therapy**. Hematopoietic **stem** cells, lymphocytes, **vascular endothelial** cells, respiratory epithelial cells, keratinocytes, skeletal and cardiac muscle cells, neurons and cancer cells are among the proposed targets for **therapeutic** gene transfer, either ex vivo or in vivo (Miller, A. D., Nature (London) 357:455-460 (1992); Miller, A. D., Curr. Top. Microbiol. Immunol. 158:1-24 (1992); Nienhuis, A. W. et al., "Viruses in **therapeutic** gene transfer vectors," in Viruses and Bone Marrow, N. S. Young, ed., Dekker, New York, N.Y. (1993), pp. 353-414; Mulligan,. . .

US PAT NO: 5,739,138 [IMAGE AVAILABLE] L5: 13 of 34

DETDESC:

DETD(63)

The . . . tumor cells and said amount is sufficient to inhibit said proliferation; or (2) a method to promote differentiation of hematopoietic **stem** cells into red blood cells, platelets, lymphocytes, and granulocytes, and said amount is sufficient to promote said proliferation; or (3). . . of stimulating said proliferation and said amount is sufficient to inhibit said proliferation; or (8) a method to lower systemic **vascular** resistance conferred by **endothelial** cells and said amount is sufficient to reduce the release of

hypertension-inducing substances; or (9) a method to lower systemic **vascular** resistance induced by **endothelial** cells and said amount is sufficient to enhance the release of anti-hypertensive substances; or (10) a method to lower expression. . . is sufficient to enhance said resistance; or (14) a method to prevent the suppression of growth stimulatory factor production in TNF-**treated** bone marrow stromal cells and said amount is sufficient to prevent said suppression; or (15) a method to prevent the. . . monocytes and macrophages; or (16) a method to prevent the release of platelet activating factor by IL-1, TNF, or endotoxin **treated** megakaryocytes, fibroblastic cells, and macrophages; or (17) a method to prevent the down-regulation of receptors for cytokines in TNF-**treated** hematopoietic **progenitor** cells and said amount is sufficient to prevent said down-regulation; or (18) a method to suppress the production of metalloproteases. . .

US PAT NO: 5,707,624 [IMAGE AVAILABLE] L5: 14 of 34

SUMMARY:

BSUM(7)

A principal obstacle in developing a **treatment** for KS has been the lack of knowledge regarding the etiology and the pathophysiology of KS. KS is characterized both by tumor cell growth and neovascularization. KS lesions contain multiple cellular constituents, including proliferating **endothelial** cells, an expanded population of dermal dendrocytes that express factor XIIIa (a transglutaminase), lymphocytes, and a population of spindle-shaped tumor. . . between these cellular constituents has not been clearly delineated. It has been hypothesized that KS tumor cells are derived from **endothelial** cells (Dorfman, R. F., Hum. Pathol. 15:1013-1017 (1984)), dermal dendrocytes (Nickoloff, B. J. et al., Am. J. Pathol. 135:793-800 (1989)), and smooth muscle cells (Weich, H. A., et al., Am. J. Pathol. 139-1251-1258 (1991)). **Endothelium**, dendrocytes, and KS tumor cells in vivo share a number of immunophenotypic features, including expression of CD34 (human **progenitor** cell antigen), **vascular** cell adhesion molecule-1 (VCAM-1), and CD31 (platelet **endothelial** cell adhesion molecule-1) (Nickoloff, B. J., Arch. Dermatol. 127:523-529 (1991) and Nickoloff, B. J., Arch Dermatol. 129:250-251 (1993)).

US PAT NO: 5,695,932 [IMAGE AVAILABLE] L5: 15 of 34

SUMMARY:

BSUM(63)

Such activators of telomerase would be useful as **therapeutic** agents to forestall and reverse cellular senescence, including but not limited to conditions associated with cellular senescence, e.g., (a) cells with replicative capacity in the central nervous system, including astrocytes, **endothelial** cells, and fibroblasts which play a role in such age-related diseases as Alzheimer's disease, Parkinson's disease, Huntington's disease, and stroke,. . . capacity in the immune system such as B and T lymphocytes, monocytes, neutrophils, eosinophils, basophils, NK cells and their respective **progenitors**, which may play a role in age-related immune system impairment, (f) cells with a finite replicative capacity in the **vascular** system including **endothelial** cells, smooth muscle cells, and adventitial fibroblasts which may play a role in age-related diseases of the **vascular** system including atherosclerosis, calcification, thrombosis, and aneurysms, and (g) cells with a finite replicative capacity in the eye such as pigmented epithelium and **vascular endothelial** cells which may play an important role in age-related macular degeneration.

US PAT NO: 5,670,506 [IMAGE AVAILABLE] L5: 16 of 34

DETDESC:

DETD(27)

The . . . tumor cells and said amount is sufficient to inhibit said proliferation; or (2) a method to promote differentiation of hematopoietic **stem** cells into red blood cells, platelets, lymphocytes, and granulocytes, and said amount is sufficient to promote said proliferation; or (3). . . of stimulating said proliferation and said amount is sufficient to inhibit said proliferation; or (8) a method to lower systemic **vascular** resistance conferred by **endothelial** cells and said amount is sufficient to reduce the release of hypertension-inducing substances; or (9) a method to lower systemic **vascular** resistance induced by **endothelial** cells and said amount is sufficient to enhance the release of anti-hypertensive substances; or (10) a method to lower expression. . . is sufficient to enhance said resistance; or (14) a method to prevent the suppression of growth stimulatory factor production in TNF-**treated** bone marrow stromal cells and said amount is sufficient to prevent said suppression; or (15) a method to prevent the. . . monocytes and macrophages; or (16) a method to prevent the release of platelet activating factor by IL-1, TNF, or endotoxin **treated** megakaryocytes, fibroblastic cells, and macrophages; or (17) a method to prevent the down-regulation of receptors for cytokines in TNF-**treated** hematopoietic **progenitor** cells and said amount is sufficient to prevent said down-regulation; or (18) a method to suppress the production of metalloproteases. . .

DETDESC:

DETD(54)

The . . . tumor cells and said amount is sufficient to inhibit said proliferation; or (2) a method to promote differentiation of hematopoietic **stem** cells into red blood cells, platelets, lymphocytes, and granulocytes, and said amount is sufficient to promote said proliferation; or (3). . . of stimulating said proliferation and said amount is sufficient to inhibit said proliferation; or (8) a method to lower systemic **vascular** resistance conferred by **endothelial** cells and said amount is sufficient to reduce the release of hypertension-inducing substances; or (9) a method to lower systemic **vascular** resistance induced by **endothelial** cells and said amount is sufficient to enhance the release of anti-hypertensive substances; or (10) a method to lower expression. . . is sufficient to enhance said resistance; or (14) a method to prevent the suppression of growth stimulatory factor production in TNF-**treated** bone marrow stromal cells and said amount is sufficient to prevent said suppression; or (15) a method to prevent the. . . monocytes and macrophages; or (16) a method to prevent the release of platelet activating factor by IL-1, TNF, or endotoxin **treated** megakaryocytes, fibroblastic cells, and macrophages; or (17) a method to prevent the down-regulation of receptors for cytokines in TNF-**treated** hematopoietic **progenitor** cells and said amount is sufficient to prevent said down-regulation; or (18) a method to suppress the production of metalloproteases. . .

US PAT NO: 5,658,892 [IMAGE AVAILABLE] L5: 17 of 34

SUMMARY:

BSUM(16)

Where . . . human patient, the method may be used in any situation where enhanced local delivery of a compound is desirable. Gene **therapy** applications such as the delivery of the Factor IIX encoding gene to **stem** cells or the delivery of the TPA genes to **vascular**

endothelia are only one class of possible applications. The methods may also be used to deliver **therapeutic** polypeptides, or other compounds of diverse molecular weights. In some cases, it will be desirable to provide multiple compounds.

US PAT NO: 5,652,243 [IMAGE AVAILABLE] L5: 18 of 34

DETDESC:

DETD(61)

The . . . tumor cells and said amount is sufficient to inhibit said proliferation; or (2) a method to promote differentiation of hematopoietic **stem** cells into red blood cells, platelets, lymphocytes, and granulocytes, and said amount is sufficient to promote said proliferation; or (3). . . of stimulating said proliferation and said amount is sufficient to inhibit said proliferation; or (8) a method to lower systemic **vascular** resistance conferred by **endothelial** cells and said amount is sufficient to reduce the release of hypertension-inducing substances; or (9) a method to lower systemic **vascular** resistance induced by **endothelial** cells and said amount is sufficient to enhance the release of anti-hypertensive substances; or (10) a method to lower expression. . . is sufficient to enhance said resistance; or (14) a method to prevent the suppression of growth stimulatory factor production in TNF-**treated** bone marrow stromal cells and said amount is sufficient to prevent said suppression; or (15) a method to prevent the. . . monocytes and macrophages; or (16) a method to prevent the release of platelet activating factor by IL-1, TNF, or endotoxin **treated** megakaryocytes, fibroblastic cells, and macrophages; or (17) a method to prevent the down-regulation of receptors for cytokines in TNF-**treated** hematopoietic **progenitor** cells and said amount is sufficient to prevent said down-regulation; or (18) a method to suppress the production of metalloproteases. . .

US PAT NO: 5,648,357 [IMAGE AVAILABLE] L5: 19 of 34

DETDESC:

DETD(65)

The . . . tumor cells and said amount is sufficient to inhibit said proliferation; or (2) a method to promote differentiation of hematopoietic **stem** cells into red blood cells, platelets, lymphocytes, and granulocytes, and said amount is sufficient to promote said proliferation; or (3). . . of stimulating said proliferation and said amount is sufficient to inhibit said proliferation; or (8) a method to lower systemic **vascular** resistance conferred by **endothelial** cells and said amount is sufficient to reduce the release of hypertension-inducing substances; or (9) a method to lower systemic **vascular** resistance induced by **endothelial** cells and said amount is sufficient to enhance the release of anti-hypertensive substances; or (10) a method to lower expression. . . is sufficient to enhance said resistance; or (14) a method to prevent the suppression of growth stimulatory factor production in TNF-**treated** bone marrow stromal cells and said amount is sufficient to prevent said suppression; or (15) a method to prevent the. . . monocytes and macrophages; or (16) a method to prevent the release of platelet activating factor by IL-1, TNF, or endotoxin **treated** megakaryocytes, fibroblastic cells, and macrophages; or (17) a method to prevent the down-regulation of receptors for cytokines in TNF-**treated** hematopoietic **progenitor** cells and said amount is sufficient to prevent said down-regulation; or (18) a method to suppress the production of metalloproteases. . .

US PAT NO: 5,645,986 [IMAGE AVAILABLE] L5: 20 of 34

SUMMARY:

BSUM(63)

Such activators of telomerase would be useful as **therapeutic** agents to forestall and reverse cellular senescence, including but not limited to conditions associated with cellular senescence, e.g., (a) cells with replicative capacity in the central nervous system, including astrocytes, **endothelial** cells, and fibroblasts which play a role in such age-related diseases as Alzheimer's disease, Parkinson's disease, Huntington's disease, and stroke,. . . capacity in the immune system such as B and T lymphocytes, monocytes, neutrophils, eosinophils, basophils, NK cells and their respective **progenitors**, which may play a role in age-related immune system impairment, (f) cells with a finite replicative capacity in the **vascular** system including **endothelial** cells, smooth muscle cells, and adventitial fibroblasts which may play a role in age-related diseases of the **vascular** system including atherosclerosis, calcification, thrombosis, and aneurysms, and (g) cells with a finite replicative capacity in the eye such as pigmented epithelium and **vascular endothelial** cells which may play an important role in age-related macular degeneration.

US PAT NO: 5,629,315 [IMAGE AVAILABLE] L5: 21 of 34

DETDESC:

DETD(59)

The . . . tumor cells and said amount is sufficient to inhibit said proliferation; or (2) a method to promote differentiation of hematopoietic **stem** cells into red blood cells, platelets, lymphocytes, and granulocytes, and said amount is sufficient to promote said proliferation; or (3). . . of stimulating said proliferation and said amount is sufficient to inhibit said proliferation; or (8) a method to lower systemic **vascular** resistance conferred by **endothelial** cells and said amount is sufficient to reduce the release of hypertension-inducing substances; or (9) a method to lower systemic **vascular** resistance induced by **endothelial** cells and said amount is sufficient to enhance the release of anti-hypertensive substances; or (10) a method to lower expression. . . is sufficient to enhance said resistance; or (14) a method to prevent the suppression of growth stimulatory factor production in TNF-**treated** bone marrow stromal cells and said amount is sufficient to prevent said suppression; or (15) a method to prevent the. . . monocytes and macrophages; or (16) a method to prevent the release of platelet activating factor by IL-1, TNF, or endotoxin **treated** megakaryocytes, fibroblastic cells, find macrophages; or (17) a method to prevent the down-regulator of receptors for cytokines in TNF-**treated** hematopoietic **progenitor** cells and said amount is sufficient to prevent said down-regulation; or (18) a method to suppress the production of metalloproteases. . .

US PAT NO: 5,621,102 [IMAGE AVAILABLE] L5: 22 of 34

DETDESC:

DETD(58)

The . . . tumor cells and said amount is sufficient to inhibit said proliferation; or (2) a method to promote differentiation of hematopoietic **stem** cells into red blood cells, platelets, lymphocytes, and granulocytes, and said amount is sufficient to promote said proliferation; or (3). . . of stimulating said proliferation and said amount is sufficient to inhibit said proliferation; or (8) a method to lower systemic **vascular** resistance conferred by **endothelial** cells and said amount is sufficient to reduce the release of

hypertension-inducing substances; or (9) a method to lower systemic **vascular** resistance induced by **endothelial** cells and said amount is sufficient to enhance the release of anti-hypertensive: substances; or (10) a method to lower expression. . . is sufficient to enhance said resistance; or (14) a method to prevent the suppression of growth stimulatory factor production in TNF-**treated** bone marrow stromal cells and said amount is sufficient to prevent said suppression; or (15) a method to prevent the. . . monocytes and macrophages; or (16) a method to prevent the release of platelet activating factor by IL-1, TNF, or endotoxin **treated** megakaryocytes, fibroblastic cells, and macrophages; or (17) a method to prevent the down-regulation of receptors for cytokines in TNF-**treated** hematopoietic **progenitor** cells and said amount is sufficient to prevent said down-regulation; or (18) a method to suppress the production of metalloproteases. . .

US PAT NO: 5,620,984 [IMAGE AVAILABLE] L5: 23 of 34

DETDESC:

DETD(58)

The . . . tumor cells and said amount is sufficient to inhibit said proliferation; or (2) a method to promote differentiation of hematopoietic **stem** cells into red blood cells, platelets, lymphocytes, and granulocytes, and said amount is sufficient to promote said proliferation; or (3). . . of stimulating said proliferation and said mount is sufficient to inhibit said proliferation; or (8) a method to lower systemic **vascular** resistance conferred by **endothelial** cells and said amount is sufficient to reduce the release of hypertension-inducing substances; or (9) a method to lower systemic **vascular** resistance induced by **endothelial** cells and said amount is sufficient to enhance the release of anti-hypertensive substances; or (10) a method to lower expression. . . is sufficient to enhance said resistance; or (14) a method to prevent the suppression of growth stimulatory factor production in TNF-**treated** bone marrow stromal cells and said amount is sufficient to prevent said suppression; or (15) a method to prevent the. . . monocytes and macrophages; or (16) a method to prevent the release of platelet activating factor by IL-1, TNF, or endotoxin **treated** megakaryocytes, fibroblastic cells, and macrophages; or (17) a method to prevent the down-regulation of receptors for cytokines in TNF-**treated** hematopoietic **progenitor** cells and said amount is sufficient to prevent said down-regulation; or (18) a method to suppress the production of metalloproteases. . .

US PAT NO: 5,612,349 [IMAGE AVAILABLE] L5: 24 of 34

DRAWING DESC:

DRWD(87)

The . . . tumor cells and said amount is sufficient to inhibit said proliferation; or (2) a method to promote differentiation of hematopoietic **stem** cells into red blood cells, platelets, lymphocytes, and granulocytes, and said amount is sufficient to promote said proliferation; or (3). . . of stimulating said proliferation and said amount is sufficient to inhibit said proliferation; or (8) a method to lower systemic **vascular** resistance conferred by **endothelial** cells and said amount is sufficient to reduce the release of hypertension-inducing substances; or (9) a method to lower systemic **vascular** resistance induced by **endothelial** cells and said amount is sufficient to enhance the release of anti-hypertensive substances; or (10) a method to lower expression. . . is sufficient to enhance said resistance; or (14) a method to prevent the suppression of growth stimulatory factor production in TNF-**treated** bone marrow stromal cells and said amount is sufficient to prevent said suppression; or (15)

a method to prevent the. . . monocytes and macrophages; or (16) a method to prevent the release of platelet activating factor by IL-1, TNF, or endotoxin **treated** megakaryocytes, fibroblastic cells, and macrophages; or (17) a method to prevent the down-regulation of receptors for cytokines in TNF-**treated** hematopoietic **progenitor** cells and said amount is sufficient to prevent said down-regulation; or (18) a method to suppress the production of metalloproteases. . .

US PAT NO: 5,583,016 [IMAGE AVAILABLE] L5: 25 of 34

SUMMARY:

BSUM(47)

Cells that can be targeted for telomerase gene **therapy** (**therapy** involving increasing the telomerase activity of a target cell) include but are not limited to hematopoietic **stem** cells (AIDS and post-chemotherapy), **vascular endothelial** cells (cardiac and cerebral **vascular** disease), skin fibroblasts and basal skin keratinocytes (wound healing and burns), chondrocytes (arthritis), brain astrocytes and microglial cells (Alzheimer's Disease),. . .

US PAT NO: 5,580,874 [IMAGE AVAILABLE] L5: 26 of 34

DETDESC:

DETD(62)

The . . . tumor cells and said amount is sufficient to inhibit said proliferation; or (2) a method to promote differentiation of hematopoietic **stem** cells into red blood cells, platelets, lymphocytes, and granulocytes, and said amount is sufficient to promote said. proliferation; or (3). . . of stimulating said proliferation and said amount is sufficient to inhibit said proliferation; or (8) a method to lower systemic **vascular** resistance conferred by **endothelial** cells and said amount is sufficient to reduce the release of hypertension-inducing substances; or (9) a method to lower systemic **vascular** resistance induced by **endothelial** cells and said amount is sufficient to enhance the release of anti-hypertensive substances; or (10) a method to lower expression. . . is sufficient to enhance said resistance; or (14) a method to prevent the suppression of growth stimulatory factor production in TNF-**treated** bone marrow stromal cells and said amount is sufficient to prevent said suppression; or (15) a method to prevent the. . . and macrophages; or (16) a method to prevent the release of platelet activating factor by IL- 1, TNF, or endotoxin **treated** megakaryocytes, fibroblastic cells, and macrophages; or (17) a method to prevent the down-regulation of receptors for cytokines in TNF-**treated** hematopoietic **progenitor** cells and said amount is sufficient to prevent said down-regulation; or (18) a method to suppress the production of metalloproteases. . .

US PAT NO: 5,580,873 [IMAGE AVAILABLE] L5: 27 of 34

DETDESC:

DETD(63)

The . . . tumor cells and said amount is sufficient to inhibit said proliferation; or (2) a method to promote differentiation of hematopoietic **stem** cells into red blood cells, platelets, lymphocytes, and granulocytes, and said amount is sufficient to promote said proliferation; or (3). . . of stimulating said proliferation and said amount is sufficient to inhibit said proliferation; or (8) a method to lower systemic **vascular** resistance conferred by **endothelial** cells and said amount is sufficient to reduce the release of

hypertension-inducing substances; or (9) a method to lower systemic **vascular** resistance induced by **endothelial** cells and said amount is sufficient to enhance the release of anti-hypertensive substances; or (10) a method to lower expression. . . is sufficient to enhance said resistance; or (14) a method to prevent the suppression of growth stimulatory factor production in TNF-**treated** bone marrow stromal cells and said amount is sufficient to prevent said suppression; or (15) a method to prevent the. . . monocytes and macrophages; or (16) a method to prevent the release of platelet activating factor by IL-1, TNF, or endotoxin **treated** megakaryocytes, fibroblastic cells, and macrophages; or (17) a method to prevent the down-regulation of receptors for cytokines in TNF-**treated** hematopoietic **progenitor** cells and said amount is sufficient to prevent said down-regulation; or (18) a method to suppress the production of metalloproteases. . .

US PAT NO: 5,567,704 [IMAGE AVAILABLE] L5: 28 of 34

DETDESC:

DETD(66)

The . . . tumor cells and said amount is sufficient to inhibit said proliferation; or (2) a method to promote differentiation of hematopoietic **stem** cells into red blood cells, platelets, lymphocytes, and granulocytes, and said amount is sufficient to promote said. proliferation; or (3). . . of stimulating said proliferation and said amount is sufficient to inhibit said proliferation; or (8) a method to lower systemic **vascular** resistance conferred by **endothelial** cells and said amount is sufficient to reduce the release of hypertension-inducing substances; or (9) a method to lower systemic **vascular** resistance induced by **endothelial** cells and said amount is sufficient to enhance the release of anti-hypertensive substances; or (10) a method to lower expression. . . is sufficient to enhance said resistance; or (14) a method to prevent the suppression of growth stimulatory factor production in TNF-**treated** bone marrow stromal cells and said amount is sufficient to prevent said suppression; or (15) a method to prevent the. . . monocytes and macrophages; or (16) a method to prevent the release of platelet activating factor by IL-1, TNF, or endotoxin **treated** megakaryocytes, fibroblastic cells, and macrophages; or (17) a method to prevent the down-regulation of receptors for cytokines in TNF-**treated** hematopoietic **progenitor** cells and said amount is sufficient to prevent said down-regulation; or (18) a method to suppress the production of metalloproteases. . .

US PAT NO: 5,521,315 [IMAGE AVAILABLE] L5: 29 of 34

DETDESC:

DETD(44)

The . . . tumor cells and said amount is sufficient to inhibit said proliferation; or (2) a method to promote differentiation of hematopoietic **stem** cells into red blood cells, platelets, lymphocytes, and granulocytes, and said amount is sufficient to promote said proliferation; or (3). . . of stimulating said proliferation and said amount is sufficient to inhibit said proliferation; or (8) a method to lower systemic **vascular** resistance conferred by **endothelial** cells and said amount is sufficient to reduce the release of hypertension-inducing substances; or (9) a method to lower systemic **vascular** resistance induced by **endothelial** cells and said amount is sufficient to enhance the release of anti-hypertensive substances; or (10) a method to lower expression. . . is sufficient to enhance said resistance; or (14) a method to prevent the suppression of growth stimulatory factor production in TNF-**treated** bone marrow stromal cells and said amount is sufficient to prevent said suppression; or (15)

a method to prevent the. . . monocytes and macrophages; or (16) a method to prevent the release of platelet activating factor by IL-1, TNF, or endotoxin **treated** megakaryocytes, fibroblastic cells, and macrophages; or (17) a method to prevent the down-regulation of receptors for cytokines in TNF-**treated** hematopoietic **progenitor** cells and said amount is sufficient to prevent said down-regulation; or (18) a method to suppress the production of metalloproteases. . .

DETDESC:

DETD(73)

The . . . tumor cells and said amount is sufficient to inhibit said proliferation; or (2) a method to promote differentiation of hematopoietic **stem** cells into red blood cells, platelets, lymphocytes, and granulocytes, and said amount is sufficient to promote said proliferation; or (3). . . of stimulating said proliferation and said amount is sufficient to inhibit said proliferation; or (8) a method to lower systemic **vascular** resistance conferred by **endothelial** cells and said amount is sufficient to reduce the release of hypertension-inducing substances; or (9) a method to lower systemic **vascular** resistance induced by **endothelial** cells and said amount is sufficient to enhance the release of anti-hypertensive substances; or (10) a method to lower expression. . . is sufficient to enhance said resistance; or (14) a method to prevent the suppression of growth stimulatory factor production in TNF-**treated** bone marrow stromal cells and said amount is sufficient to prevent said suppression; or (15) a method to prevent the. . . monocytes and macrophages; or (16) a method to prevent the release of platelet activating factor by IL-1, TNF, or endotoxin **treated** megakaryocytes, fibroblastic cells, and macrophages; or (17) a method to prevent the down-regulation of receptors for cytokines in TNF-**treated** hematopoietic **progenitor** cells and said amount is sufficient to prevent said down-regulation; or (18) a method to suppress the production of metalloproteases. . .

US PAT NO: 5,470,878 [IMAGE AVAILABLE] L5: 30 of 34

DETDESC:

DETD(45)

The . . . to growth factors capable of stimulating said proliferation and said amount is sufficient to inhibit said proliferation; (6) lower systemic **vascular** resistance conferred by **endothelial** cells and said amount is sufficient to reduce the release of hypertension-inducing substances; (7) lower systemic **vascular** resistance induced by **endothelial** cells and said amount is sufficient to enhance the release of anti-hypertensive substances; (8) lower expression of adhesion molecules induced. . . TNF, or endotoxin stimulated monocytes and macrophages; (13) prevent the release of platelet activating factor by IL-1, TNF, or endotoxin **treated** megakaryocytes, fibroblastic cells, and macrophages; (14) prevent the down-regulation of receptors for cytokines in TNF-**treated** hematopoietic **progenitor** cells and said amount is sufficient to prevent said down-regulation; (15) suppress the production of metalloproteases in IL-1-stimulated or TNF-stimulated. . .

DETDESC:

DETD(85)

The . . . inhibit the proliferation of smooth muscle cells in response to growth factors capable of stimulating said proliferation (6) lower systemic **vascular** resistance conferred by **endothelial** cells, (7) lower systemic **vascular** resistance induced by

endothelial cells, (8) lower expression of adhesion molecules induced by enhancers thereof, (9) suppress the activation of T-cells and macrophages by. . . TNF, or endotoxin stimulated monocytes and macrophages; (13) prevent the release of platelet activating factor by IL-1, TNF, or endotoxin **treated** megakaryocytes, fibroblastic cells, and macrophages; (14) prevent the down-regulation of receptors for cytokines in TNF-**treated** hematopoietic **progenitor** cells, (15) suppress the production of metalloproteases in IL-1-stimulated or TNF-stimulated glomerular epithelial cells or synovial cells, (16) enhance the. . .

US PAT NO: 5,440,041 [IMAGE AVAILABLE] L5: 31 of 34

DETDESC:

DETD(39)

The . . . tumor cells and said amount is sufficient to inhibit said proliferation; or (2) a method to promote differentiation of hematopoietic **stem** cells into red blood cells, platelets, lymphocytes, and granulocytes, and said amount is sufficient to promote said proliferation; or (3). . . of stimulating said proliferation and said amount is sufficient to inhibit said proliferation; or (8) a method to lower systemic **vascular** resistance conferred by **endothelial** cells and said amount is sufficient to reduce the release of hypertension-inducing substances; or (9) a method to lower systemic **vascular** resistance induced by **endothelial** cells and said amount is sufficient to enhance the release of anti-hypertensive substances; or (10) a method to lower expression. . . is sufficient to enhance said resistance; or (14) a method to prevent the suppression of growth stimulatory factor production in TNF-**treated** bone marrow stromal cells and said amount is sufficient to prevent said suppression; or (15) a method to prevent the. . . monocytes and macrophages; or (16) a method to prevent the release of platelet activating factor by IL-1, TNF, or endotoxin **treated** megakaryocytes, fibroblastic cells, and macrophages; or (17) a method to prevent the down-regulation of receptors for cytokines in TNF-**treated** hematopoietic **progenitor** cells and said amount is sufficient to prevent said down-regulation; or (18) a method to suppress the production of metalloproteases. . .

US PAT NO: 5,428,070 [IMAGE AVAILABLE] L5: 32 of 34

SUMMARY:

BSUM(33)

Once . . . like. Alternatively, the NO synthase construct within viral vectors may be introduced by standard infection techniques. For somatic cell gene **therapy**, autologous cells will generally be employed, although in some instances allogeneic cells or recombinantly modified cells may be employed. Usually the cells employed for genetic modification will be mature **endothelial** or **vascular** smooth muscle cells. Occasionally, the cells employed for genetic modification will be **progenitor** cells, particularly early **progenitor** cells. For example, myoblasts may be employed for muscle cells or hematopoietic **stem** cells or high proliferative potential cells may be employed for lymphoid and/or myelomonocytic cells.

US PAT NO: 5,416,195 [IMAGE AVAILABLE] L5: 33 of 34

SUMMARY:

BSUM(2)

The . . . represent a vital factor in response to infection. In this

regard granulocytes can extend pseudopods and slip out of the **vascular** tree between the lining **endothelial** cells. The neutrophilic granulocytes can then come into direct contact with the microorganisms and destroy them using unique enzyme systems. . . . in the circulation (approximately 6-12 hours) and are destroyed in the course of their function, it is necessary for the **stem** cells of the bone marrow to generate as many granulocytes as red blood cells each day. Further, this rate of. . . to overwhelming infection. Indeed sepsis is a common cause of death in cancer patients whose marrow is suppressed by radiation **treatment**, chemotherapy or their neoplastic disease.

US PAT NO: 5,354,756 [IMAGE AVAILABLE] L5: 34 of 34

DETDESC:

DETD(39)

The . . . tumor cells and said amount is sufficient to inhibit said proliferation; or (2) a method to promote differentiation of hematopoietic **stem** cells into red blood cells, platelets, lymphocytes, and granulocytes, and said amount is sufficient to promote said proliferation; or (3). . . of stimulating said proliferation and said mount is sufficient to inhibit said proliferation; or (8) a method to lower systemic **vascular** resistance conferred by **endothelial** cells and said amount is sufficient to reduce the release of hypertension-inducing substances; or (9) a method to lower systemic **vascular** resistance induced by **endothelial** cells and said amount is sufficient to enhance the release of anti-hypertensive substances; or (10) a method to lower expression. . . is sufficient to enhance said resistance; or (14) a method to prevent the suppression of growth stimulatory factor production in TNF-**treated** bone marrow stromal cells and said amount is sufficient to prevent said suppression; or (15) a method to prevent the. . . monocytes and macrophages; or (16) a method to prevent the release of platelet activating factor by IL-1, TNF, or endotoxin **treated** megakaryocytes, fibroblastic cells, and macrophages; or (17) a method to prevent the down-regulation of receptors for cytokines in TNF-**treated** hematopoietic **progenitor** cells and said amount is sufficient to prevent said down-regulation; or (18) a

Set	Items	Description
S1	83	E1-E4
S2	2	S1 AND (PROGENITOR? OR STEM)
S3	2	RD S2 (unique items)
S4	253	ENDOTHELIAL AND (PROGENITOR? OR STEM) AND (NEOVASCULARI? OR ANGIOGEN? OR ISCHEM?)
S5	149	RD S4 (unique items)
S6	0	S S5 AND (ISOLAT? OR PURIFIED)(10N)(STEM OR PROGENITOR?)
S7	0	S S5 AND (ISOLAT? OR PURIFIED)
S8	7	S5 AND (ADMINISTER? OR ADMINISTRAT?)
S9	7	RD S8 (unique items)
S10	114	S5 AND (ENDOTHELIAL)(5N)(CELL? OR PROGENITOR? OR STEM)

? t s10/7/8,11,15,18,25,31,34,17,47,53,71,74,84,85,108,110

10/7/8 (Item 8 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

10954447 BIOSIS NO.: 199799575592
Phenotypic diversity and lineage relationships in vascular **endothelial cells**.
BOOK TITLE: **Stem** cells

AUTHOR: Schor Ana M; Schor Seth L; Arciniegas Enrique
BOOK AUTHOR/EDITOR: Potten C S: Ed
AUTHOR ADDRESS: Dep. Dent. Surgery Periodontology, Univ. Dundee, Dundee, UK
p119-146 1997

10/7/11 (Item 11 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

10830378 BIOSIS NO.: 199799451523
Isolation of putative **progenitor endothelial cells** for **angiogenesis**.

AUTHOR: Asahara Takayuki; Murohara Toyoaki; Sullivan Alison; Silver Marcy; Van Der Zee Rien; Li Tong; Witzenbichler Bernhard; Schatteman Gina; Isner Jeffrey M(a)
AUTHOR ADDRESS: (a)Dep. Biomed. Res., St. Elizabeth's Med. Center, Tufts Univ. Sch. Med., 736 Cambridge St., Boston, USA

JOURNAL: Science (Washington D C) 275 (5302):p964-967 1997

ABSTRACT: Putative **endothelial cell** (EC) **progenitors** or angioblasts were isolated from human peripheral blood by magnetic bead selection on the basis of cell surface antigen expression. In vitro, these cells differentiated into ECs. In animal models of **ischemia**, heterologous, homologous, and autologous EC **progenitors** incorporated into sites of active **angiogenesis**. These findings suggest that EC **progenitors** may be useful for augmenting collateral vessel growth to **ischemic** tissues (therapeutic **angiogenesis**) and for delivering anti- or pro-**angiogenic** agents, respectively, to

sites of pathologic or utilitarian **angiogenesis**.

10/7/15 (Item 15 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

10681496 BIOSIS NO.: 199799302641
Blood **cell** drived **endothelial cell** precursor can participate in **angiogenesis** in vivo.

AUTHOR: Asahara Takayuki; Schatteman Gina; Sullivan Alison; Silver Marcy; Isner Jefferey M
AUTHOR ADDRESS: St. Elizabeth's Med. Cent., Boston, MA, USA

JOURNAL: Circulation 94 (8 SUPPL.):pI237 1996

10/7/18 (Item 18 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

10635952 BIOSIS NO.: 199699257097
Embryonic **stem cells** differentiate in vitro to **endothelial cells** through successive maturation steps.

AUTHOR: Vittet Daniel(a); Prandini Marie-Helene; Berthier Rolande; Schweitzer Annie; Martin-Sisteron Herve; Uzan Georges; Dejana Elisabetta
AUTHOR ADDRESS: (a)INSERM U217, DBMS/HEM, CENG, 17 rue des Martyrs, 38054 Grenoble cedex 9, France

JOURNAL: Blood 88 (9):p3424-3431 1996

ABSTRACT: The mechanisms involved in the regulation of vasculogenesis still remain unclear in mammals. Totipotent embryonic **stem** (ES) cells may represent a suitable in vitro model to study molecular events involved in vascular development. In this study, we followed the expression kinetics of a relatively large set of **endothelial**-specific markers in ES-derived ambryoid bodies (EBs). Results of both reverse transcription-polymerase chain reaction and/or immunofluorescence analysis show that a spontaneous **endothelial** differentiation occurs during EBs development. ES-derived **endothelial cells** express a full range of **cell** lineage-specific markers: platelet **endothelial cell** adhesion molecule (PECAM), Flk-1, tie-1, tie-2, vascular **endothelial** (VE) cadherin, MECA-32, and MEC14.7, Analysis of the kinetics of **endothelial** marker expression allows the distinction of successive maturation steps. Flk-1 was the first to be detected; its mRNA is apparent from day 3 of differentiation. PECAM and tie-2 mRNAs were found to be expressed only from day 4, whereas VE-cadherin and tie-1 mRNAs cannot be detected before day 5. Immunofluorescence stainings of EBs with antibodies directed against Flk-1, PECAM, VE-cadherin, MECA-32, and MEC-14.7 confirmed that the expression of these antigens occurs at different steps of **endothelial cell** differentiation. The addition of an **angiogenic** growth factor mixture including erythropoietin, interleukin-6, fibroblast growth factor 2, and vascular **endothelial** growth factor in the EB culture medium significantly increased the development of primitive vascular-like structures within EBs. These results indicate that this in vitro system contains a large part of the **endothelial cell** differentiation program and constitutes a suitable model to study the molecular mechanisms involved in vasculogenesis.

10/7/25 (Item 25 from file: 55)

DIALOG(R)File 55:BIOSIS PREVIEWS(R)
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10169132 BIOSIS NO.: 199698624050
Dose-dependent induction of **endothelial cells** from embryonic **stem cells** using vascular permeability factor (VPF/VEGF).

AUTHOR: Reimer C L; Van De Water L
AUTHOR ADDRESS: Dep. Pathol., Beth Israel Hosp., Harv. Med. Sch., Boston, MA, USA

JOURNAL: Molecular Biology of the Cell 6 (SUPPL.):p10A 1995

10/7/31 (Item 31 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)
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09633882 BIOSIS NO.: 199598088800
Transformation of fibroblasts into **endothelial cells** during **angiogenesis**.

AUTHOR: Kon Kazunori; Fujiwara Takashi(a)
AUTHOR ADDRESS: (a)Lab. Animal Center, Sch. Med., Ehime Univ., Shigenobu, Ehime 791-02, Japan

JOURNAL: Cell & Tissue Research 278 (3):p625-628 1994

ABSTRACT: Light- and electron-microscopic autoradiography have been used to study fibroblast transformation into **endothelial cells** in the formation of new blood vessels during wound healing in rabbit ear chambers. When cultured fibroblasts labeled with tritium thymidine were transplanted autologously into the chambers, newly formed blood vessels contained **endothelial cells** labeled with tritium thymidine. This result suggests that fibroblasts play a pivotal role in **angiogenesis**, as **progenitors** of **endothelial cells** in newly formed blood vessels.

10/7/34 (Item 34 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)
(c) 1998 BIOSIS. All rts. reserv.

09156244 BIOSIS NO.: 199497164614
Regulation of vasculogenesis and **angiogenesis**.

AUTHOR: Risau Werner
AUTHOR ADDRESS: Max-Planck-Inst., D-61231 Bad Nauheim, Germany

JOURNAL: Journal of Cellular Biochemistry Supplement 0 (18 PART A):p260 1994

10/7/17 (Item 17 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)
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10666563 BIOSIS NO.: 199799287708
Cell autonomous functions of the receptor tyrosine kinase TIE in a late phase of **angiogenic** capillary growth and **endothelial cell** survival during murine development.

AUTHOR: Partanen Juha; Puri Mira C; Schwartz Lois; Fischer Klaus-Dieter; Bernstein Alan; Rossant Janet(a)
AUTHOR ADDRESS: (a)Programs Mol. Biol. Cancer, Samuel Lunenfeld Res. Inst.,

Mount Sinai Hosp., 600 University Ave.,, Canada

JOURNAL: Development (Cambridge) 122 (10):p3013-3021 1996

ABSTRACT: TIE is a receptor tyrosine kinase expressed in both mature **endothelial cells** and their precursors, as well as in some hematopoietic cells. Mouse embryos homozygous for a disrupted Tie allele die at midgestation due to impaired **endothelial cell** integrity and resulting hemorrhage. Here we have performed chimeric analysis to study further the function of the murine TIE in the development of embryonic vasculature and in the hematopoietic system. Cells lacking a functional Tie gene (tie-lcz/tie-lczn- cells) contributed to the embryonic vasculature at E10.5 as efficiently as cells heterozygous for a targeted Tie allele (tie-lcz/+ cells). Thus, TIE does not play a significant role in vasculogenesis or in early **angiogenic** processes, such as formation of the intersomitic arteries and limb bud vascularization. At E15.5 tie-lczn- cells still readily contributed to major blood vessels and to **endothelial cells** of organs such as lung and heart, which have been suggested to be vascularized by angioblast differentiation. In contrast, the tie-lcz/tie-lczn- cells were selected against in the capillary plexuses of several **angiogenically** vascularized tissues, such as brain and kidney. Our results thus support a role for TIE in late phases of **angiogenesis** but not vasculogenesis. Furthermore, the results suggest that different mechanisms regulate early and late **angiogenesis** and provide support for a model of differential organ vascularization by vasculogenic or **angiogenic** processes. Analysis of adult chimeras suggested that TIE is required to support the survival or proliferation of certain types of **endothelial cells** demonstrating heterogeneity in the growth/survival factor requirements in various **endothelial cell** populations. Chimeric analysis of adult hematopoietic cell populations, including peripheral platelets and bone marrow **progenitor** cells, revealed that tie-lcz/tie-lczn- cells were able to contribute to these cell types in a way indistinguishable from tielczl+ or wild-type cells. Thus, the primary function of TIE appears to be restricted to the **endothelial cell** lineage.

10/7/47 (Item 9 from file: 72)
DIALOG(R)File 72:EMBASE

10582314 EMBASE No: 98009887
TAL1/SCL is expressed in **endothelial progenitor cells** /angioblasts and defines a dorsal-to-ventral gradient of vasculogenesis
Drake C.J.; Brandt S.J.; Trusk T.C.; Little C.D.
C.J. Drake, Department of Cell Biology, Cardiovasc. Devtl. Biology Center, Medical University of South Carolina, Charleston, SC 29425 United States
Developmental Biology (United States) , 1997, 192/1 (17-30)
CODEN: DEBIA ISSN: 0012-1606
DOCUMENT TYPE: Journal ; Article
LANGUAGES: ENGLISH SUMMARY LANGUAGES: ENGLISH
NUMBER OF REFERENCES: 50
In this study we establish that TAL1/SCL, a member of the helix-loop-helix family of transcription factors, and an important regulator of the hematopoietic lineage in mice, is expressed in the **endothelial** lineage of avians. The earliest events of vascular development were examined using antibodies to TAL1/SCL, and the QH1 antibody, an established marker of quail **endothelial cells** . Analyses using double immunofluorescence confocal microscopy show that: (i) TAL1/SCL is expressed by both quail and chicken **endothelial cells**; (ii) TAL1/SCL expression precedes that of the QH1 epitope; and (iii) TAL1/SCL, but not QH1, expression defines a subpopulation of primordial cells within the splanchnic mesoderm. Collectively these data suggest that

TAL1/SCL-positive/QH1-negative cells are angioblasts. Further, using TAL1/SCL expression as a marker of the **endothelial** lineage, we demonstrate that in addition to the previously described cranial-to-caudal gradient, there is a dorsal-to-ventral progression of vasculogenesis.

10/7/53 (Item 15 from file: 72)
DIALOG(R)File 72:EMBASE

10409080 EMBASE No: 97213623
Regulation of tie receptor expression on human **endothelial cells** by protein kinase C-mediated release of soluble tie
Yabkowitz R.; Meyer S.; Yanagihara D.; Brankow D.; Staley T.; Elliott G.; Hu S.; Ratzkin B.
Dr. R. Yabkowitz, Mammalian Cell Molecular Biology, M/S 14-2-C, Amgen Inc, 1840 DeHavilland Dr, Thousand Oaks, CA 91320-1789 USA
Blood (USA) , 1997, 90/2 (706-715)
CODEN: BLOOA ISSN: 0006-4971
DOCUMENT TYPE: Journal
LANGUAGES: English SUMMARY LANGUAGES: English
NUMBER OF REFERENCES: 49
The expression and activity of receptor tyrosine kinases (RTK) at the cell surface can be modulated by several different pathways including the proteolytic release of the extracellular domain as a soluble receptor. We investigated the regulation of tie receptor expression, an orphan RTK restricted to **cells** of hematopoietic and **endothelial** lineages, on primary human **endothelial cells** and a stably transfected Chinese hamster ovary (CHO) cell line. Tie was expressed in cells as a doublet of 135 and 125 kD; the 135-kD band represented mature cell surface receptor containing sialic acid and N-linked oligosaccharide residues, whereas the 125-kD band represented an intracellular pool of immature receptor. Phorbol 12-myristate 13-acetate (PMA) had dramatic effects on tie expression at the cell surface. Within 15 minutes of PMA treatment, the 135-kD band disappeared from the cell surface and was accompanied by the appearance of a 100-kD band in cell supernatants. The 100-kD band continued to accumulate in the media throughout the duration of PMA treatment during which mature tie receptor was undetectable on the cell surface by fluorescence-activated cell sorting (FACS) or in cell lysates by immunoblot analysis. Using specific antibodies, this 100-kD species was shown to be a soluble form of the tie receptor containing the extracellular domain. PMA-dependent release of soluble tie was mediated through the activation of protein kinase C (PKC); soluble tie was not released in the presence of PKC inhibitors, an inactive PMA analog, or following the downregulation of PKC through chronic PMA treatment. These results indicate that tie receptor expression on **endothelial cells** is regulated by the release of a soluble extracellular fragment following activation of PKC. Parallel pathways regulating c-kit, tumor necrosis factor (TNF), and colony-stimulating factor (CSF) receptor expression suggest that the release of extracellular receptor fragments represents an alternative mechanism through which cells modulate responses to growth factors and cytokines.

10/7/71 (Item 33 from file: 72)
DIALOG(R)File 72:EMBASE

8910279 EMBASE No: 93214049
Flk-1, an fit-related receptor tyrosine kinase is an early marker for **endothelial cell** precursors
Yamaguchi T.P.; Dumont D.J.; Conlon R.A.; Breitman M.L.; Rossant J.
Samuel Lunenfeld Research Instltute, Mount Sinai Hospital, Toronto, Ont. M5G 1X5 Canada
DEVELOPMENT (United Kingdom) , 1993, 118/2 (489-498)
CODEN: DEVPE ISSN: 0950-1991

LANGUAGES: English SUMMARY LANGUAGES: English

10/7/74 (Item 36 from file: 72)
DIALOG(R)File 72:EMBASE

7790231 EMBASE No: 90219551
Leukocyte antigen CD34 is expressed by a subset of cultured **endothelial cells** and on **endothelial** abluminal microprocesses in the tumor stroma
Schlingemann R.O.; Rietveld F.J.R.; De Waal R.M.W.; Bradley N.J.; Skene A.I.; Davies A.J.S.; Greaves M.F.; Denekamp J.; Ruiter D.J.
Department of Pathology, University Hospital Nijmegen, P.O. Box 9101, 6500 HB Nijmegen Netherlands
LAB. INVEST. (USA) , 1990, 62/6 (690-696)
CODEN: LAINA ISSN: 0023-6837
LANGUAGES: English
It has been reported that the human haemopoietic **progenitor** cell antigen CD34 is also expressed by vascular structures. To investigate its precise vascular localization, we have studied the cellular and subcellular distribution of CD34 in normal tissues and pathologic tissues with **neovascularization** . In normal resting tieeuse, anti-CD34 antibodies. ICH3 and QBEND-10 predominantly stain the luminal **endothelial** membrane, whereas the abluminal membrane is negative or weakly positive. In contrast, a striking staining of **endothelial** abluminal microprocesses (EAM) was found in the tumor stroma. These structures, measuring up to 20 microm in length, could be observed in thick vibratome sections both at the tips of vascular sprouts and, also frequently, on fully formed microvessels. The number of vascular sprouts and EAM varied widely between different tumors. CD34-stained EAM were sparsely present in fetal tissue of 10 weeks gestation, but they could not be demonstrated in granulation tissue of wound healing. By immunoelectron microscopy, the EAM were continuous with the cytoplasm of **endothelial cells** showing an immature phenotype as seen in regeneration. In cultured human umblilical vein endothelium, CD34 was preferentially found on a small subset of cells with the morphologic appearance of migrating cells. These findings suggest that CD34 is an **endothelial** marker for EAM present during **angiogenesis**.

10/7/84 (Item 8 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

09080427 97314981
Colonization of neural allografts by host microglial cells: relationship to graft **neovascularization**.
Pennell NA; Streit WJ
Department of Neuroscience, University of Florida Brain Institute, Gainesville 32610, USA.
Cell Transplant (UNITED STATES) May-Jun 1997, 6 (3) p221-30, ISSN 0963-6897 Journal Code: B02
Languages: ENGLISH
Document type: JOURNAL ARTICLE
In order to illuminate functional roles of microglial cells within neural allografts, we have transplanted both whole and microglial and **endothelial cell**-depleted E14 neural **cell** suspensions into the intact striatum of Sprague-Dawley rats. Following posttransplantation times of up to 30 days, the intrastrial allografts were analyzed histochemically using the Griffonia simplicifolia B4 isolectin, a marker for both microglia and blood vessels. Our results indicate that both whole and depleted suspension grafts develop identically in terms of **neovascularization** and microglial colonization. In both types of transplants microglial cells appeared before any blood vessels were

apparent. The main phase of graft vascularization occurred between days 7 and 10 posttransplantation and **neovascularization** was complete by day 21, as revealed by quantitative image analysis. Microglial cells, which were present as ameboid cells during early posttransplantation times, underwent continuing cell differentiation with time that paralleled graft vascular development. By 30 days posttransplantation microglia within the grafts had assumed the fully ramified phenotype characteristic of resting adult microglia. During graft development and vascularization, microglia were often seen in close proximity to ingrowing blood vessels and vascular sprouts. In conclusion, our study has shown that microglial colonization of grafts and graft vascularization occurs independent of donor-derived microglial and **endothelial cells**, and suggests that the great majority of microglia and vessels within the graft are host derived. We hypothesize that the host microglia invading the allografts play an active role in promoting graft **neovascularization**.

10/7/85 (Item 9 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

09026434 97286336
Vascular development: cellular and molecular regulation.
Beck L Jr; D'Amore PA
Department of Pathology, Harvard Medical School, Children's Hospital, Boston, Massachusetts 02115, USA.
FASEB J (UNITED STATES) Apr 1997, 11 (5) p365-73, ISSN 0892-6638 Journal Code: FAS
Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW; REVIEW LITERATURE
The vascular system forms through a combination of vasculogenesis and **angiogenesis** . In vasculogenesis, vessels form de novo via the assembly of **endothelial** precursors called angioblasts, whereas in **angiogenesis** new vessels arise by migration and proliferation of **endothelial cells** from preexisting vessels. Although the two processes are distinct in some respects, recent evidence suggests that they share a number of regulatory mechanisms. The identification of a number of defined growth factors, observations of genetically manipulated mice, and the recognition of the importance of cell-cell interactions have greatly expanded our understanding of the regulation of vascularization. The paracrine actions of a variety of polypeptide growth factors, including platelet-derived growth factor, vascular **endothelial** growth factor, transforming growth factor-beta, and the angiopoietins, appear to be orchestrated in a complex sequence of steps that lead to the development of the adult vascular system. Thus, communication between the forming vasculature and the tissue parenchyma, as well as interactions among cells of the vascular wall, all appear to influence vascular development and growth. (67 Refs.)

10/7/108 (Item 2 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

128242083 CA: 128(20)242083h JOURNAL
Endothelial progenitor cells for neovascularization
AUTHOR(S): Asahara, Takayuki; Takahashi, Tomono; Isner, Jeffery M.
LOCATION: Sch. Med., Tufts Univ., Boston, 02135, USA
JOURNAL: Jikken Igaku DATE: 1998 VOLUME: 16 NUMBER: 5 PAGES: 605-611
CODEN: JIIGEF ISSN: 0288-5514 LANGUAGE: Japanese PUBLISHER: Yodosha
SECTION:
CA213000 Mammalian Biochemistry
CA214XXX Mammalian Pathological Biochemistry
IDENTIFIERS: review endothelial progenitor cell neovascularization
DESCRIPTORS:

Hematopoietic stem cell...
    angioblast; endothelial progenitor cells for neovascularization
Angiogenesis... Vascular endothelium...
    endothelial progenitor cells for neovascularization

10/7/110 (Item 4 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

127159382 CA: 127(12)159382p JOURNAL
Isolation of endothelial progenitor cell for angiogenesis
AUTHOR(S): Asahara, Takayuki
LOCATION: St. Elizabeth's Med. Cent., Tufts Univ. Sch. Med., Boston, 02135, USA
JOURNAL: Jikken Igaku DATE: 1997 VOLUME: 15 NUMBER: 12 PAGES: 1507-1510 CODEN: JIIGEF ISSN: 0288-5514 LANGUAGE: Japanese PUBLISHER: Yodosha
SECTION:
CA213000 Mammalian Biochemistry
IDENTIFIERS: review angiogenesis vasculogenesis endothelial progenitor cell
DESCRIPTORS:
Hematopoietic precursor cell...
    endothelial; isolation and therapeutic application of endothelial progenitor cell for angiogenesis
Angiogenesis... Blood vessel...
    isolation and therapeutic application of endothelial progenitor cell for angiogenesis
?
PLEASE ENTER A COMMAND OR BE LOGGED OFF IN 5 MINUTES
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TIMEOUT: Logged Off 11/08/98 11:05:29 by System

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Dialog level 98.09.24D

Last logoff:  07nov98 12:32:39
Logon file001 08nov98 10:36:29
ANNOUNCEMENT   ****    ANNOUNCEMENT   ****    ANNOUNCEMENT
NEW
***French Patents (File 371) - November 2, 1998

***CorpTech (File 559)
***Gannett News Service (File 604)
***UMI Newsstand(TM) (File 781)
***Baton Rouge Advocate (File 382)
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***LA Times (File 630)
***Research Centers and Services (File 115)
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***IAC Industry Express (File 12) - merged into IAC PROMT (file 16)
***UPI News archival (File 260)
***Federal Register (File 669 - replaced by File 180)
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***** *** File 220 is currently unavailable. ***
***** *** File 196 is currently unavailable. ***
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File   1:ERIC  1966-1998/Jul
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      Set  Items  Description
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? b 410

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? set hi ;set hi

       08nov98 10:36:36 User208760 Session D1138.1
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     $0.30  Estimated cost File1
            FTSNET   0.016 Hrs.
     $0.30  Estimated cost this search
     $0.30  Estimated total session cost   0.093 DialUnits

File 410:Chronolog(R)  1981-1998/Nov/Dec
       (c) 1998 The Dialog Corporation plc

      Set  Items  Description
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?
HILIGHT set on as ''
HILIGHT set on as ''
? begin 55,72,154,399,351

       08nov98 10:36:53 User208760 Session D1138.2
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            FTSNET   0.004 Hrs.
     $0.00  Estimated cost this search
     $0.30  Estimated total session cost   0.134 DialUnits

SYSTEM:OS  - DIALOG OneSearch
  File  55:BIOSIS PREVIEWS(R)  1993-1998/Oct W4
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      Set  Items  Description
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? e au=isner, jeffrey ?


Ref   Items  Index-term
E1        2  AU=ISNER, JEFFERY M.
E2        2  AU=ISNER, JEFFREY
E3        0 *AU=ISNER, JEFFREY ?
E4       79  AU=ISNER, JEFFREY M.
E5        1  AU=ISNER, PAMELA D.
E6        2  AU=ISNER, R. JOSEPH
E7        3  AU=ISNER, WILLIAM G.
E8        1  AU=ISNES J
E9        1  AU=ISNETSOV VV
E10       1  AU=ISNIEWSKI H.M.
E11       1  AU=ISNIK F E
E12       1  AU=ISNIKAWA N

          Enter P or PAGE for more
? s e1-e4
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              2  AU=ISNER, JEFFERY M.
              2  AU=ISNER, JEFFREY
              0  AU=ISNER, JEFFREY ?
             79  AU=ISNER, JEFFREY M.
      S1     83  E1-E4
? s s1 and (progenitor? or stem)

             83  S1
          43485  PROGENITOR?
         178330  STEM
      S2      2  S1 AND (PROGENITOR? OR STEM)
? rd s2

>>>Duplicate detection is not supported for File 351.

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...completed examining records
      S3      2  RD S2 (unique items)
? t s3/7/all


 3/7/1     (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
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  129008577    CA: 129(1)8577w    PATENT
  Methods for regulating angiogenesis
  INVENTOR(AUTHOR): Isner, Jeffrey M.; Asahara, Takayuki
  LOCATION: USA
  ASSIGNEE: St. Elizabeth's Medical Center of Boston, Inc.
  PATENT: PCT International ; WO 9819712 A1  DATE: 19980514
  APPLICATION: WO 97US19935 (19971106) *US 744882 (19961108)
  PAGES: 57 pp.  CODEN: PIXXD2  LANGUAGE: English  CLASS: A61K-048/00A;
A61K-035/12B; C12N-005/10B; A61K-047/00B; A61K-049/00B
  DESIGNATED COUNTRIES: AU; CA; JP  DESIGNATED REGIONAL: AT; BE; CH; DE; DK
; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE
  SECTION:
CA263005 Pharmaceuticals
CA202XXX Mammalian Hormones
  IDENTIFIERS: angiogenesis inhibitor stimulator therapy
  DESCRIPTORS:
CD34(antigen)...
    -pos. mononuclear cell; methods for regulating angiogenesis
Tumors(animal)...
    angiogenesis-dependent; methods for regulating angiogenesis
Angiogenic factors... Growth inhibitors(animal)...
    angiogenic growth-inhibiting factors; methods for regulating
    angiogenesis
Mononuclear cell(leukocyte)...
    CD34-pos.; methods for regulating angiogenesis
Nucleic acids...
    endothelial cell mitogen-encoding; methods for regulating angiogenesis
Neovascularization...
    eye; methods for regulating angiogenesis
Angioplasty...
    injury from; methods for regulating angiogenesis
Arm... Leg...
    ischemia; methods for regulating angiogenesis
Cardiomyopathy...
    ischemic; methods for regulating angiogenesis
Angiogenesis inhibitors... Angiogenesis... Antirheumatic drugs... Antitumor
agents... Catheters... Cerebral ischemia... Cytotoxic agents... Diabetic
retinopathy... Drug delivery systems... Hepatocyte growth factor... Lung
ischemia... Mitogens... Myocardial ischemia... Platelet-derived growth
factors... Psoriasis... Renal ischemia... Rheumatoid arthritis... Syringes
```

... Transforming growth factor .alpha.... Transforming growth factors .beta.... Tumor necrosis factor .alpha....
    methods for regulating angiogenesis
Glaucoma(disease)...
    neovascular; methods for regulating angiogenesis
Eye diseases...
    neovascularization; methods for regulating angiogenesis
Platelet-derived growth factors...
    platelet-derived endothelial growth factor; methods for regulating angiogenesis
Vascular endothelium...
    progenitor; methods for regulating angiogenesis
Medical goods...
    stents, injury from endovascular; methods for regulating angiogenesis
Vascular injury...
    treatment of; methods for regulating angiogenesis
  CAS REGISTRY NUMBERS:
11096-26-7 61912-98-9 62229-50-9 62683-29-8 81627-83-0 83869-56-1
    106096-92-8 106096-93-9 125978-95-2 127464-60-2 methods for regulating angiogenesis

 3/7/2   (Item 2 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

  128242083   CA: 128(20)242083h   JOURNAL
  Endothelial progenitor cells for neovascularization
  AUTHOR(S): Asahara, Takayuki; Takahashi, Tomono; Isner, Jeffery M.
  LOCATION: Sch. Med., Tufts Univ., Boston, 02135, USA
  JOURNAL: Jikken Igaku DATE: 1998 VOLUME: 16 NUMBER: 5 PAGES: 605-611
  CODEN: JIIGEF ISSN: 0288-5514 LANGUAGE: Japanese PUBLISHER: Yodosha
  SECTION:
CA213000 Mammalian Biochemistry
CA214XXX Mammalian Pathological Biochemistry
  IDENTIFIERS: review endothelial progenitor cell neovascularization
  DESCRIPTORS:
Hematopoietic stem cell...
    angioblast; endothelial progenitor cells for neovascularization
Angiogenesis... Vascular endothelium...
    endothelial progenitor cells for neovascularization
? s endothelial and (progenitor? or stem) and (neovasculari? or angiogen? or ischem?)

          147129 ENDOTHELIAL
           43485 PROGENITOR?
          178330 STEM
           15829 NEOVASCULARI?
           23798 ANGIOGEN?
          234311 ISCHEM?
      S4   253 ENDOTHELIAL AND (PROGENITOR? OR STEM) AND (NEOVASCULARI? OR ANGIOGEN? OR ISCHEM?)
? rd s4

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...examined 50 records (100)
...examined 50 records (150)
...examined 50 records (200)
...examined 50 records (250)
...completed examining records
      S5   149 RD S4 (unique items)
? s s s5 and (isolat? or purified)(10n)(stem or progenitor?)

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        1215728  ISOLAT?
         312711  PURIFIED
         178330  STEM
          43485  PROGENITOR?
           5235  (ISOLAT? OR PURIFIED)(10N)(STEM OR PROGENITOR?)
     S6       0  S S5 AND (ISOLAT? OR PURIFIED)(10N)(STEM OR PROGENITOR?)
? s s s5 and (isolat? or purified)

              0  S S5
        1215728  ISOLAT?
         312711  PURIFIED
     S7       0  S S5 AND (ISOLAT? OR PURIFIED)
? s s5 and (administer? or administrat?)

            149  S5
         331076  ADMINISTER?
        1374371  ADMINISTRAT?
     S8       7  S5 AND (ADMINISTER? OR ADMINISTRAT?)
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>>>Duplicate detection is not supported for File 351.

>>>Records from unsupported files will be retained in the RD set.
...completed examining records
     S9       7  RD S8 (unique items)
? t s9/7/all


 9/7/1     (Item 1 from file: 55)
DIALOG(R)File  55:BIOSIS PREVIEWS(R)
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11621262   BIOSIS NO.: 199800403314
In vivo radioprotective effects of angiogenic growth factors on the
  small bowel of C3H mice.

AUTHOR: Okunieff Paul(a); Mester Marcelo; Wang Jian; Maddox Theresa; Gong
  Xiaoqi; Tang Dalia; Coffee Megan; Ding Ivan(a)
AUTHOR ADDRESS: (a)Dep. Radiation Onco9l., Univ. Rochester Sch. Med. Dent.,
  601 Elmwood Avenue, Box 647, Rochester,, USA

JOURNAL: Radiation Research  150 (2):p204-211 Aug., 1998

ABSTRACT: This study was undertaken to determine if acidic or basic
  fibroblast growth factor (FGF1 or FGF2) or vascular endothelial
  growth factor (VEGF) alters the radiation response of small bowel after
  total-body irradiation (TBI). Female C3H mice were treated with various
  doses of angiogenic growth factor administered intravenously
  24 h before or 1 h after TBI. Radiation doses ranged from 7 to 18 Gy. End
  points measured were the number of crypts in three portions of the small
  bowel, the frequency of apoptosis of crypt cells at various times after
  TBI, and the LD50/30 (bone marrow syndrome) and LD50/6 (GI syndrome).
  Fibroblast growth factors alone, without TBI, decreased the number of
  crypts per circumference significantly. Among the factors tested, FGF2
  caused the greatest decline in baseline crypt number. Despite this
  decrease in the baseline crypt number, after irradiation the number of
  surviving crypts was greater in animals treated with growth factor. The
  greatest radioprotection occurred at intermediate doses of growth factor
  (6 to 18 pg/mouse). Mice treated with FGF1 and FGF2 had crypt survival
  curves with a slope that was more shallow than that for saline-treated
  animals, indicating radiation resistance of crypt stem cells in
  FGF-treated mice. The LD50/6 was increased by approximately 10% for all
  treatments with angiogenic growth factors, whether given before or
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after TBI. Apoptosis of crypt cells was maximum at 4 to 8 h after TBI. The cumulative apoptosis was decreased significantly in animals treated with **angiogenic** growth factors, and the greatest protection against apoptosis was seen in animals treated with FGF2 prior to TBI. All three **angiogenic** growth factors tested were radioprotective in small bowel whether given 24 h before or 1 h after irradiation. The mechanism of protection is unlikely to involve proliferation of crypt **stem** cells, but probably does involve prevention of radiation-induced apoptosis or enhanced repair of DNA damage of crypt cells.

9/7/2 (Item 2 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

10183105 BIOSIS NO.: 199698638023
Time course of increased cellular proliferation in collateral arteries after **administration** of vascular **endothelial** growth factor in a rabbit model of lower limb vascular insufficiency.

AUTHOR: Takeshita Satoshi; Rossow Susan T; Kearney Marianne; Zheng Lu P; Bauters Christophe; Bunting Stuart; Ferrara Napoleone; Symes James F; Isner Jeffrey M(a)
AUTHOR ADDRESS: (a)St. Elizabeth's Med. Cent., 736 Cambridge Street, Boston, MA 02135, USA

JOURNAL: American Journal of Pathology 147 (6):p1649-1660 1995

ABSTRACT: Proliferation of vascular cells has been previously shown to contribute to spontaneous development of coronary collaterals. Recent studies from several laboratories have established that collateral artery growth in both the heart and limb can be enhanced by **administration** of **angiogenic** growth factors, or therapeutic **angiogenesis**. In this study, we sought (1) to define the extent and time course of **endothelial** cell (EC) and smooth muscle cell (SMC) proliferation accompanying spontaneous collateral development during limb **ischemia** and (2) to determine the extent to which proliferative activity of ECs and SMCs is augmented during therapeutic **angiogenesis** with vascular **endothelial** growth factor (VEGF), a heparin-binding EC-specific mitogen. Ten days after induction of limb **ischemia** by surgically excising the femoral artery of rabbits, either VEGF (500 to 1000 mu-g) or saline was **administered** as a bolus into the iliac artery of the **ischemic** limb. Cellular proliferation was evaluated by bromodeoxyuridine labeling for 24 hours at day 0 (immediately before VEGF **administration**) and at days 3, 5, and 7 after VEGF. EC proliferation in the midzone collaterals of VEGF-treated animals increased 2.8-fold at day 5 (P lt 0.05 versus control), and returned to baseline levels by day 7. SMC proliferation in midzone collaterals also increased 2.7-fold in response to VEGF (P lt 0.05). No significant increase in EC or SMC proliferation was observed in either the **stem** or re-entry collateral of VEGF-treated animals compared with untreated **ischemic** control animals. Reduction of hemodynamic deficit in the **ischemic** limb measured by lower limb blood pressure wets documented at day 7 after VEGF (P lt 0.01 versus untreated, **ischemic** control). These data thus (1) establish the contribution of cellular proliferation to collateral vessel development in limb **ischemia** and (2) support the concept that augmented cellular proliferation contributes to the enhanced formation of collateral vessels after therapeutic **angiogenesis** with VEGF.

9/7/3 (Item 3 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

10156469 BIOSIS NO.: 199698611387
Synergistic effect of vascular **endothelial** growth factor and basic fibroblast growth factor on **angiogenesis** in vivo.

AUTHOR: Asahara Takayuki; Bauters Christophe; Zheng Lu P; Takeshita Satoshi ; Bunting Stuart; Ferrara Napoleone; Symes James F(a); Isner Jeffrey M
AUTHOR ADDRESS: (a)St. Elizabeth's Med. Cent., Med. Off. Build., 11 Nevins St. Suite No. 306, Boston, MA 02135, USA

JOURNAL: Circulation 92 (9 SUPPL.):pII365-II371 1995

ABSTRACT: Background: Recent studies have suggested that vascular **endothelial** growth factor (VEGF) and basic fibroblast growth factor (bFGF) may have synergistic effects on the induction of **angiogenesis** in vitro. Therefore, we investigated the hypothesis that the simultaneous **administration** of VEGF and bFGF, each having been previously shown to independently enhance collateral development in an animal model of hind limb **ischemia**, could have a synergistic effect in vivo. Methods and Results: Ten days after surgical induction of unilateral hind limb **ischemia**, New Zealand White rabbits were randomized to receive either VEGF 500 mu-g alone (n=6), bFGF 10 mu-g alone (n=7), VEGF 500 mu-g, immediately followed by 10 mu-g bFGF (n=7), or vehicle only (control animals, n=8) in each case **administered** intra-arterially via a catheter in the internal iliac artery of the **ischemic** limb. BP ratio (BPR, **ischemic**/healthy limb) at day 10 for the VEGF+bFGF group was 0.82 +- 0.01, much superior (P lt .0005) to that of either the VEGF group (0.52 +- 0.02) or the bFGF group (0.57 +- 0.02). This outcome persisted at day 30: BPR in the VEGF+bFGF group (0.91 +- 0.02) exceeded that of the control group (0.49+-0.05, P lt .0001), the VEGF group (0.65 +- 0.03, P lt .0005), or the bFGF group (0.66 +- 0.03, P lt .0005). Serial angiography demonstrated a progressive increase in luminal diameter of the **stem** collateral artery and the number of opacified collaterals in the thigh of the **ischemic** limbs in all groups. **Stem** artery diameter with VEGF+bFGF (1.34 +- 0.07 mm) on day 30 was significantly (P lt .05) greater than with either VEGF (1.09 +- 0.09) or bFGF (1.18 +- 0.06) alone. Capillary density was significantly greater (P lt .05) in VEGF+bFGF animals (275 +- 20 mm-2) compared with VEGF (201+-8) or bFGF (209 +- 15). Conclusions: Combined **administration** of VEGF and bFGF stimulates significantly greater and more rapid augmentation of collateral circulation, resulting in superior hemodynamic improvement compared with either VEGF or bFGF alone. This synergism of two **angiogenic** mitogens with different target cell specificities may have important implications for the treatment of severe arterial insufficiency in patients whose disease is not amenable to direct revascularization.

9/7/4 (Item 4 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

09169851 BIOSIS NO.: 199497178221
Therapeutic **angiogenesis**: A single intraarterial bolus of vascular **endothelial** growth factor augments revascularization in a rabbit **ischemic** hind limb model.

AUTHOR: Takeshita Satoshi; Zheng Lu P; Brogi Edi; Kearney Marianne; Pu Li-Qun; Bunting Stuart; Ferrara Napoleone; Symes James F; Isner Jeffrey M (a)
AUTHOR ADDRESS: (a)St. Elizabeth's Medical Cent., 736 Cambridge St., Boston, MA 02135, USA

JOURNAL: Journal of Clinical Investigation 93 (2):p662-670 1994

ABSTRACT: Vascular **endothelial** growth factor (VEGF) is a

heparin-binding, **endothelial** cell-specific mitogen. Previous studies have suggested that VEGF is a regulator of naturally occurring physiologic and pathologic **angiogenesis**. In this study we investigated the hypothesis that the **angiogenic** potential of VEGF is sufficient to constitute a therapeutic effect. The soluble 165 amino acid isoform of VEGF was **administered** as a single intraarterial bolus to the internal iliac artery of rabbits in which the ipsilateral femoral artery was excised to induce severe, unilateral hind limb **ischemia**. Doses of 500-1,000 mu-g of VEGF produced statistically significant augmentation of collateral vessel development by angiography as well as the number of capillaries by histology; consequent amelioration of the hemodynamic deficit in the **ischemic** limb was significantly greater in animals receiving VEGF than in nontreated controls (calf blood pressure ratio, 0.75 +- 0.14 vs. 0.48 +- 0.19, P lt 0.05). Serial angiograms disclosed progressive linear extension of the collateral artery of origin (**stem** artery) to the distal point of parent vessel (reentry artery) reconstitution in seven of nine VEGF-treated animals. These findings establish proof of principle for the concept that the **angiogenic** activity of VEGF is sufficiently potent to achieve therapeutic benefit. Such a strategy might ultimately be applicable to patients with severe limb **ischemia** secondary to arterial occlusive disease.

9/7/5 (Item 1 from file: 72)
DIALOG(R)File 72:EMBASE

9811259 EMBASE No: 95367134

Time course of increased cellular proliferation collateral arteries after **administration** of vascular **endothelial** growth factor in a rabbit model of lower limb vascular insufficiency

Takeshita S.; Rossow S.T.; Kearney M.; Zheng L.P.; Bauters C.; Bunting S.; Ferrara N.; Symes J.F.; Isner J.M.

St. Elizabeths Medical Center, 736 Cambridge Street, Boston, MA 02135 USA

American Journal of Pathology (USA) , 1995, 147/6 (1649-1660)
CODEN: AJPAA ISSN: 0002-9440
LANGUAGES: English SUMMARY LANGUAGES: English

Proliferation of vascular cells has been previously shown to contribute to spontaneous development of coronary collaterals. Recent studies from several laboratories have established that collateral artery growth in both the heart and limb can be enhanced by **administration** of **angiogenic** growth factors, or therapeutic **angiogenesis**. In this study, we sought (1) to define the extent and time course of **endothelial** cell (EC) and smooth muscle cell (SMC) proliferation accompanying spontaneous collateral development during limb **ischemia** and (2) to determine the extent to which proliferarive activity of ECs and SMCs is augmented during therapeutic **angiogenesis** with vascular **endothelial** growth factor (VEGF), a heparin-binding EC-specific mitogen. Ten days after induction of limb **ischemia** by surgically excising the femoral artery of rabbits, either VEGF (500 to 1000 microg) or saline was **administered** as a bolus into the iliac artery of the **ischemic** limb. Cellular proliferation was evaluated by bromodeoxyuridine labeling for 24 hours at day 0 (immediately before VEGF **administration**) and at days 3, 5, and 7 after VEGF. EC proliferation in the midzone collaterals of VEGF-treated animals increased 2.8-fold at day 5 ($P < 0.05$ versus control), and returned to baseline levels by day 7. SMC proliferation in midzone collaterals also increased 2.7-fold in response to VEGF ($P < 0.05$). No significant increase in EC or SMC proliferation was observed in either the **stem** or re-entry collaterals of VEGF-treated animals compared with untreated **ischemic** control animals. Reduction of hemodynamic deficit in the **ischemic** limb measured by lower limb blood pressure was documented at day 7 after VEGF ($P < 0.01$ versus untreated, **ischemic** control). These data thus (1)

establish the contribution of cellular proliferation to collateral vessel development in limb **ischemia** and (2) support the concept that augmented cellular proliferation contributes to the enhanced formation of collateral vessels after therapeutic **angiogenesis** with VEGF.

9/7/6 (Item 1 from file: 351)
DIALOG(R)File 351:DERWENT WPI

011869696
WPI Acc No: 98-286606/199825
Using **endothelial progenitor** cells for therapeutic regulation of **angiogenesis** - e.g. to treat tumours of ischaemia, also for treating injured blood vessels and to detect ischaemic tissue or injured vessels in vivo
Patent Assignee: ST ELIZABETH'S MEDICAL CENT BOSTON INC (SELI-N)
Inventor: ASAHARA T; ISNER J M
Number of Countries: 020 Number of Patents: 002
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Main IPC	Week
WO 9819712	A1	19980514	WO 97US19935	A	19971106	A61K-048/00	199825 B
AU 9852432	A	19980529	AU 9852432	A	19971106	A61K-048/00	199841

Priority Applications (No Type Date): US 96744882 A 19961108
Patent Details:

Patent	Kind	Lan	Pg	Filing Notes	Application	Patent
WO 9819712	A1	E	56			
	Designated States (National): AU CA JP					
	Designated States (Regional): AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
AU 9852432	A			Based on		WO 9819712

Abstract (Basic): WO 9819712 A

Use of optically modified **endothelial progenitor** cells (EPC) for therapeutic regulation of **angiogenesis** is new. Also new are: (1) use of EPC for treating injured blood vessels, and (2) use of labelled EPC for detecting ischaemic tissue or vascular injury.

To reduce **angiogenesis**, EPC carry, or have been engineered to express, a cytotoxin or **angiogenesis** inhibitor, e.g. O-chloroacetylcarbamoyl fumagillol, thrombospondin, angiostatin, diptheria toxin, ricin A chain, etc. To increase **angiogenesis**, EPC may express an EC mitogen, specifically acidic or basic fibroblast growth factor (GF), vascular **endothelial** GF (VEGF), epidermal GF, transforming growth factor alpha or beta , platelet-derived (**endothelial**) GF, tumour necrosis factor alpha , hepatocyte GF, insulin-like GF, erythropoietin, (granulocyte)macrophage colony stimulating factor ((G)MCSF) or nitric oxide synthase, especially VEGF. In method (1), EPD are used with a (I) or are modified to express (I). EPC are isolated from peripheral or umbilical cord blood or bone marrow, particularly the leucocyte fraction of peripheral blood. Isolation uses an antibody directed against an EPC-specific antigen, particularly CD34.

USE - EPC are used to reduce or enhance **angiogenesis**, depending on how they are modified. Reduction is useful for treating rheumatoid arthritis, psoriasis, ocular **neovascularisation**, diabetic retinopathy, neovascular glaucoma or **angiogenesis** -dependent tumours and metastates, while enhancement is useful in cases of ischaemia (cerebrovascular, renal, pulmonary, myocardial or of a limb) or ischaemic cardiomyopathy. Method (1) is particularly used where injury is caused by balloon angioplasty or by positioning of a stent; it causes re-endothelialisation of the vessel so indirectly reduces restenosis by inhibition of smooth muscle proliferation. EPC can also be engineered to improve the immune response to disease or tumours, e.g. by expression of Interleukin-2 (IL-2). Cells are

administered at 106-108 per dose,particularly to selected sites via a catheter. When EPC are used to carry DNA, this is 1-4000 (preferably 2000-4000) mu g.

ADVANTAGE - EPC allow precise targeting to injured blood vessels and regions of **angiogenesis** (so reduce side effects); can be manipulated genetically and differentiate in vivo to **endothelial** cells (EC).

Dwg.0/9

Derwent Class: B04; D16
International Patent Class (Main): A61K-048/00
International Patent Class (Additional): A61K-035/12; A61K-047/00; A61K-049/00; C12N-005/10

9/7/7 (Item 2 from file: 351)
DIALOG(R)File 351:DERWENT WPI

011834381
WPI Acc No: 98-251291/199822
New fibroblast growth factor homologue, zFGF-5 - used to develop products for treating e.g. heart failure, stroke, hypertension, bone defects or cancers, arthritis, or wounds
Patent Assignee: ZYMOGENETICS INC (ZYMO)
Inventor: BUKOWSKI T R; CONKLIN D C; DEISHER T A; HANSEN B; HOLDERMAN S D; RAYMOND F C; SHEPPARD P O
Number of Countries: 075 Number of Patents: 002
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Main IPC	Week
WO 9816644	A1	19980423	WO 97US18635	A	19971016	C12N-015/18	199822 B
AU 9747583	A	19980511	AU 9747583	A	19971016	C12N-015/18	199837

Priority Applications (No Type Date): US 9628646 A 19961016
Patent Details:

Patent	Kind	Lan	Pg	Filing Notes	Application	Patent
WO 9816644	A1	E	94			
AU 9747583	A			Based on	WO 9816644	

Designated States (National): AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG UZ VN
Designated States (Regional): AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW

Abstract (Basic): WO 9816644 A

An isolated polynucleotide (PN) molecule (A) is claimed which encodes a fibroblast growth factor (FGF) homologue polypeptide selected from:(a) a PN comprising nucleotides 82-621 of a 917 bp sequence given in the specification; (b) allelic variants of (a); (c) a PN molecule that encode a polypeptide that is at least 60% identical to residues 28-207 of a 207 amino acid (aa) sequence given in the specification; and (d) PN molecules comprising nucleotides 82-621 of a 621bp sequence given in the specification. Also claimed are: (1) an expression vector comprising the following operably linked elements: (a) a transcription promoter; (b) a DNA segment selected from PN molecules as in (A) (a)-(d); (c) a transcription terminator; (2) a cultured cell containing an expression vector as in (2), where the cell expresses a polypeptide encoded by the DNA segment; (3) an isolated FGF homologue polypeptide selected from: (a) polypeptide molecules comprising from residue 28 (Glu) to residue 1 75 (Met) or to residue 196 (Lys) or to residue 207 (Ala) of a 207 aa sequence given in the specification; (b) allelic variants of (a); and (c) polypeptide molecules that are at least 60% identical to a sequence as in (a); (4) an antibody that binds to an epitope of a polypeptide molecule comprising an amino acid sequence from residue 1 (Met) to residue 207 (Ala) of a 207 aa sequence given in

the specification; and (5) a method of delivering an agent or drug selectively to heart tissue comprising: (a) linking a first molecule comprising an FGF homologue polypeptide with a second molecule comprising an agent or drug to form a chimera; and (b) **administering** the chimera to heart tissue.

USE - The novel FGF homologue is designated zFGF-5. The zFGF-5 polypeptides can be used (optionally ex vivo) for enhancing the proliferation of cardiac tissue cells, such as myocytes or myocyte **progenitors** (both claimed) or myoblasts, skeletal myocytes or myoblasts and smooth muscle cells, chondrocytes, **endothelial** cells, adipocytes and osteoblasts in vitro. The polypeptides, nucleic acids and antibodies can also be used in the treatment of disorders associated with myocardial infarction, congestive heart failure, hypertrophic cardiomyopathy and dilated cardiomyopathy, for limiting infarct size following a heart attack, promoting **angiogenesis** and wound healing following angioplasty or endarterectomy, to develop coronary collateral circulation, for revascularisation in the eye, for complications related to poor circulation such as diabetic foot ulcers, for stroke, following coronary reperfusion and other indications where **angiogenesis** is of benefit, for improving cardiac function, either by inducing cardiac myocyte neogenesis and/or hyperplasia, by inducing coronary collateral formation, or by inducing remodelling of necrotic myocardial area, for the induction of skeletal muscle neogenesis and/or hyperplasia, kidney regeneration and/or for treatment of systemic and pulmonary hypertension. The products can also be used to promote the repair of bone defects and deficiencies, such as those occurring in closed, open and non-union fractures, to promote bone healing in plastic surgery, to stimulate bone ingrowth into non-cemented prosthetic joints and dental implants, in the treatment of periodontal disease and defects, to increase bone formation during distraction osteogenesis, and in treatment of other skeletal disorders that may be treated by stimulation of osteoblastic activity, such as osteooporosis and arthritis. Antagonists to zFGF-5 can be used in the treatment of e.g. rhabdomyosarcoma, cardiac myxoma, bone cancers of osteoblast origin, and dwarfism, arthritis, ligament and cartilage repair. The products can also be used in the study of cardiac myocyte hyperplasia and regeneration, to target delivery of agents to the heart and for detection and diagnosis. The recombinant cells can be used to produce the protein (claimed).

Dwg.0/3

Derwent Class: B04; D16
International Patent Class (Main): C12N-015/18
International Patent Class (Additional): A61K-038/18; C07K-014/50; C07K-016/22; C07K-019/00; C12N-005/10

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? ds

Set     Items   Description
S1         83   E1-E4
S2          2   S1 AND (PROGENITOR? OR STEM)
S3          2   RD S2 (unique items)
S4        253   ENDOTHELIAL AND (PROGENITOR? OR STEM) AND (NEOVASCULARI? OR
                ANGIOGEN? OR ISCHEM?)
S5        149   RD S4 (unique items)
S6          0   S S5 AND (ISOLAT? OR PURIFIED)(10N)(STEM OR PROGENITOR?)
S7          0   S S5 AND (ISOLAT? OR PURIFIED)
S8          7   S5 AND (ADMINISTER? OR ADMINISTRAT?)
S9          7   RD S8 (unique items)
? s s5 and (endothelial(5n)(cell? or progenitor? or stem)

>>>Unmatched parentheses
? s s5 and (endothelial)(5n)(cell? or progenitor? or stem)

Processing
Processing
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            149  S5
         147129  ENDOTHELIAL
        5080680  CELL?
          43485  PROGENITOR?
         178330  STEM
         111469  ENDOTHELIAL(5N)((CELL? OR PROGENITOR?) OR STEM)
    S10     114  S5 AND (ENDOTHELIAL)(5N)(CELL? OR PROGENITOR? OR STEM)
? t s10/3/all


 10/3/1     (Item 1 from file: 55)
DIALOG(R)File  55:BIOSIS PREVIEWS(R)
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11619839   BIOSIS NO.: 199800401810
Stem cell factor induction is associated with mast cell accumulation
  after canine myocardial ischemia and reperfusion.

AUTHOR: Frangogiannis Nikolaos G; Perrard Jerry L; Mendoza Leonardo H;
  Burns Alan R; Lindsey Merry L; Ballantyne Christie M; Michael Lloyd H;
  Smith C Wayne; Entman Mark L(a)
AUTHOR ADDRESS: (a)Dep. Med., Cardiovasc., Baylor Coll. Med., One Baylor
  Plaza, M/S F-602, Houston, TX 77030-3498, USA

JOURNAL: Circulation  98 (7):p687-698 Aug. 18, 1998
ISSN: 0009-7322


 10/3/2     (Item 2 from file: 55)
DIALOG(R)File  55:BIOSIS PREVIEWS(R)
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11304469   BIOSIS NO.: 199800085801
Endothelial cells in chorionic fetal vessels of first trimester
  placenta express HLA-G.

AUTHOR: Blaschitz Astrid; Lenfant Francoise; Mallet Valerie; Hartmann
  Michaele; Bensussan Armand; Geraghty Daniel E; Le Bouteiller Philippe(a);
  Dohr Gottfried
AUTHOR ADDRESS: (a)INSERM U395, CHU Purpan, BP 3028, F-31024 Toulouse Cedex
  3, France

JOURNAL: European Journal of Immunology  27 (12):p3380-3388 Dec., 1997
ISSN: 0014-2980


 10/3/3     (Item 3 from file: 55)
DIALOG(R)File  55:BIOSIS PREVIEWS(R)
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11251285   BIOSIS NO.: 199800032617
The LKLF transcription factor is required for normal tunica media formation
  and blood vessel stabilization during murine embryogenesis.

AUTHOR: Kuo Chay T; Veselits Margaret L; Barton Kevin P; Lu Min Min;
  Clendenin Cynthia; Leiden Jeffrey M(a)
AUTHOR ADDRESS: (a)Committee Genetics Dep. Med. Pathol., Univ. Chicago,
  Chicago, IL 60637, USA

JOURNAL: Genes & Development  11 (22):p2996-3006 Nov. 15, 1997
ISSN: 0890-9369


 10/3/4     (Item 4 from file: 55)
DIALOG(R)File  55:BIOSIS PREVIEWS(R)
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11236153 BIOSIS NO.: 199800017485
Vasculogenesis, developed by **endothelial progenitor cells** , has significant role in **neovascularization** in severe **ischemia**.

AUTHOR: Asahara Takayuki; Takahashi Tomono; Silver Marcy; Li Tong; Yang Jihong
AUTHOR ADDRESS: St. Elizabeth's Med. Cent., Boston, MA, USA

JOURNAL: Circulation 96 (8 SUPPL.):pI415-I416 10/21/97, 1997
ISSN: 0009-7322

10/3/5 (Item 5 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)
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11181837 BIOSIS NO.: 199799802982
Beta-1 integrin is essential for teratoma growth and **angiogenesis**.

AUTHOR: Bloch Wilhelm; Forsberg Erik; Lentini Sylvia; Brakebusche Cord; Martin Karl; Krell Hans W; Weidle Ulrich H; Addicks Klaus; Faessler Reinhard(a)
AUTHOR ADDRESS: (a)Max Planck Inst. Biochem., am Klopferspitz 18 A, 82 152 Martinsried, Germany

JOURNAL: Journal of Cell Biology 139 (1):p265-278 1997
ISSN: 0021-9525

10/3/6 (Item 6 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)
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11128754 BIOSIS NO.: 199799749899
CD34 expression patterns during early mouse development are related to modes of blood vessel formation and reveal additional sites of hematopoiesis.

AUTHOR: Wood Heather B; May Gillian; Healy Lyn; Enver Tariq; Morriss-Kay Gillian M(a)
AUTHOR ADDRESS: (a)Dep. Human Anat., South Parks Rd., Oxford OX1 3QX, UK

JOURNAL: Blood 90 (6):p2300-2311 1997
ISSN: 0006-4971

10/3/7 (Item 7 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)
(c) 1998 BIOSIS. All rts. reserv.

10989504 BIOSIS NO.: 199799610649
Proto-oncogene of int-3, a mouse Notch homologue, is expressed in **endothelial cells** during early embryogenesis.

AUTHOR: Shirayoshi Yasuaki(a); Yuasa Yoshihiro; Suzuki Takashi; Sugaya Kimihiko; Kawase Eihachiro; Ikemura Toshimichi; Nakatsuji Norio
AUTHOR ADDRESS: (a)Mammalian Dev. Lab., Natl. Inst. Genet., 1111 Yata, Mishima 411, Japan

JOURNAL: Genes To Cells 2 (3):p213-224 1997
ISSN: 1356-9597

10/3/8 (Item 8 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

10954447 BIOSIS NO.: 199799575592
Phenotypic diversity and lineage relationships in vascular **endothelial cells**.
BOOK TITLE: **Stem** cells

AUTHOR: Schor Ana M; Schor Seth L; Arciniegas Enrique
BOOK AUTHOR/EDITOR: Potten C S: Ed
AUTHOR ADDRESS: Dep. Dent. Surgery Periodontology, Univ. Dundee, Dundee, UK
p119-146 1997

10/3/9 (Item 9 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

10941570 BIOSIS NO.: 199799562715
Human cytotrophoblasts adopt a vascular phenotype as the differentiate: A strategy for successful endovascular invasion?

AUTHOR: Zhou Yan; Fisher Susan J; Janatpour Mary; Genbacev Olga; Dejana Elisabetta; Wheelock Margaret; Damsky Caroline H(a)
AUTHOR ADDRESS: (a)HSW 604 UCSF, 513 Parnassus Ave., San Francisco, CA 94143-0512, USA

JOURNAL: Journal of Clinical Investigation 99 (9):p2139-2151 1997
ISSN: 0021-9738

10/3/10 (Item 10 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

10912850 BIOSIS NO.: 199799533995
CD34 is involved in **endothelial cell** apoptosis and **angiogenesis**.

AUTHOR: Zhang Dan Ning; Khush Kiran K; Romero Luz I; Chan Vincent T; Abrams Kevin; Hultquist Kevin L; Herron G Scott
AUTHOR ADDRESS: Dep. Dermatol., Stanford Univ. Sch. Med., Stanford, CA, USA

JOURNAL: Journal of Investigative Dermatology 108 (4):p581 1997
ISSN: 0022-202X

10/3/11 (Item 11 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

10830378 BIOSIS NO.: 199799451523
Isolation of putative **progenitor endothelial cells** for **angiogenesis**.

AUTHOR: Asahara Takayuki; Murohara Toyoaki; Sullivan Alison; Silver Marcy; Van Der Zee Rien; Li Tong; Witzenbichler Bernhard; Schatteman Gina; Isner Jeffrey M(a)
AUTHOR ADDRESS: (a)Dep. Biomed. Res., St. Elizabeth's Med. Center, Tufts Univ. Sch. Med., 736 Cambridge St., Boston, USA

JOURNAL: Science (Washington D C) 275 (5302):p964-967 1997
ISSN: 0036-8075

10/3/12 (Item 12 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

10784160 BIOSIS NO.: 199799405305
Constitutive production and thrombin-induced release of vascular **endothelial** growth factor by human megakaryocytes and platelets.

AUTHOR: Mohle Robert; Green David; Moore Malcolm A S; Nachman Ralph L; Rafii Shahin(a)
AUTHOR ADDRESS: (a)Div. Hematol. Oncol., Cornell Univ. Med. Coll., 1300 York Ave., Room C-616 New York, NY 10021, USA

JOURNAL: Proceedings of the National Academy of Sciences of the United States of America 94 (2):p663-668 1997
ISSN: 0027-8424

10/3/13 (Item 13 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

10722440 BIOSIS NO.: 199799343585
Vectors for cancer gene therapy.

AUTHOR: Zhang J; Russell S J(a)
AUTHOR ADDRESS: (a)Cambridge Cent. Protein Eng., MRC Cent., Hills Road, Cambridge CB2 2QH, UK

JOURNAL: Cancer and Metastasis Reviews 15 (3):p385-401 1996
ISSN: 0167-7659

10/3/14 (Item 14 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

10707513 BIOSIS NO.: 199799328658
ELK and LERK-2 in developing kidney and microvascular **endothelial** assembly.

AUTHOR: Daniel Thomas O(a); Stein Elke; Cerretti Douglas P; St John Patricia L; Robert Barry; Abrahamson Dale R
AUTHOR ADDRESS: (a)Nephrology Div., MCN S3223, Vanderbilt Univ., Nashville, TN 37232-2372, USA

JOURNAL: Kidney International Supplement 0 (57):pS73-S81 1996
ISSN: 0098-6577

10/3/15 (Item 15 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

10681496 BIOSIS NO.: 199799302641
Blood **cell** drived **endothelial cell** precursor can participate in **angiogenesis** in vivo.

AUTHOR: Asahara Takayuki; Schatteman Gina; Sullivan Alison; Silver Marcy; Isner Jefferey M
AUTHOR ADDRESS: St. Elizabeth's Med. Cent., Boston, MA, USA

JOURNAL: Circulation 94 (8 SUPPL.):pI237 1996
ISSN: 0009-7322

10/3/16 (Item 16 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

10671179 BIOSIS NO.: 199799292324
Enhanced CD34 expression of sinusoid-like vascular **endothelial cells** in hepatocellular carcinoma.

AUTHOR: Cui Shunjin(a); Hano Hiroshi; Sakata Akihiko; Harada Toru; Liu Tiecheng; Takai Shigeharu; Ushigome Shinichiro
AUTHOR ADDRESS: (a)Dep. Pathol., Jikei Univ. Sch. Med., 3-25-8 Nishi-Shinbashi, Minato-ku, Tokyo 105, Japan

JOURNAL: Pathology International 46 (10):p751-756 1996
ISSN: 1320-5463

10/3/17 (Item 17 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

10666563 BIOSIS NO.: 199799287708
Cell autonomous functions of the receptor tyrosine kinase TIE in a late phase of **angiogenic** capillary growth and **endothelial cell** survival during murine development.

AUTHOR: Partanen Juha; Puri Mira C; Schwartz Lois; Fischer Klaus-Dieter; Bernstein Alan; Rossant Janet(a)
AUTHOR ADDRESS: (a)Programs Mol. Biol. Cancer, Samuel Lunenfeld Res. Inst., Mount Sinai Hosp., 600 University Ave.,, Canada

JOURNAL: Development (Cambridge) 122 (10):p3013-3021 1996
ISSN: 0950-1991

10/3/18 (Item 18 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

10635952 BIOSIS NO.: 199699257097
Embryonic **stem cells** differentiate in vitro to **endothelial cells** through successive maturation steps.

AUTHOR: Vittet Daniel(a); Prandini Marie-Helene; Berthier Rolande; Schweitzer Annie; Martin-Sisteron Herve; Uzan Georges; Dejana Elisabetta
AUTHOR ADDRESS: (a)INSERM U217, DBMS/HEM, CENG, 17 rue des Martyrs, 38054 Grenoble cedex 9, France

JOURNAL: Blood 88 (9):p3424-3431 1996
ISSN: 0006-4971

10/3/19 (Item 19 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

10575922 BIOSIS NO.: 199699197067
Regulation of flt-1 expression during mouse embryogenesis suggests a role in the establishment of vascular endothelium.

AUTHOR: Fong Guo-Hua(a); Klingensmith John; Wood Clive R; Rossant Janet; Breitman Martin L
AUTHOR ADDRESS: (a)Lawson Res. Inst., St. Joseph's Health Centre, 268 Grosvenor St., London, ON N6A 4V2, Canada

JOURNAL: Developmental Dynamics 207 (1):p1-10 1996
ISSN: 1058-8388

10/3/20 (Item 20 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

10493810 BIOSIS NO.: 199699114955
Differentiation of vascular **endothelial cells** and megakaryocytes from mouse embryonic **stem** cells transferred with TGF-beta gene (ES-T).

AUTHOR: Zhang Xue Jun; Tsung Hsiao-Chien; Li Xiu Lan; Yao Zhen; Han Zhong Chao
AUTHOR ADDRESS: Shanghai Inst. Cell Biol., Acad. Sinica, Paris, France

JOURNAL: British Journal of Haematology 93 (SUPPL. 2):p148 1996
ISSN: 0007-1048

10/3/21 (Item 21 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

10320712 BIOSIS NO.: 199698775630
Heterozygous embryonic lethality induced by targeted inactivation of the VEGF gene.

AUTHOR: Ferrara Napoleone(a); Carver-Moore Karen(a); Chen Helen(a); Dowd Mary(a); Lu Lucy(a); O'Shea K Sue; Powell-Braxton Lyn(a); Hillan Kenneth J(a); Moore Mark W(a)
AUTHOR ADDRESS: (a)Dep. Cardiovasc. Res., Genentech Inc., 460 Point San Bruno Boulevard, South San Francisco, CA 94, USA

JOURNAL: Nature (London) 380 (6573):p439-442 1996
ISSN: 0028-0836

10/3/22 (Item 22 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

10219424 BIOSIS NO.: 199698674342
Myeloid **progenitor cell** regulatory effects of vascular **endothelial cell** growth factor.

AUTHOR: Broxmeyer Hal E(a); Cooper Scott; Li Zhi Hua; Lu Li; Song Ho-Yeong; Kwon Byoung Se; Warren Robert E; Donner David B
AUTHOR ADDRESS: (a)Walther Oncol. Cent., Indiana Univ. Sch. Med., 975 West Walnut St., Room 501, Indianapolis, IN 4, USA

JOURNAL: International Journal of Hematology 62 (4):p203-215 1995
ISSN: 0925-5710

10/3/23 (Item 23 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

10183105 BIOSIS NO.: 199698638023
Time course of increased cellular proliferation in collateral arteries after administration of vascular **endothelial** growth factor in a rabbit model of lower limb vascular insufficiency.

AUTHOR: Takeshita Satoshi; Rossow Susan T; Kearney Marianne; Zheng Lu P; Bauters Christophe; Bunting Stuart; Ferrara Napoleone; Symes James F; Isner Jeffrey M(a)
AUTHOR ADDRESS: (a)St. Elizabeth's Med. Cent., 736 Cambridge Street, Boston, MA 02135, USA

JOURNAL: American Journal of Pathology 147 (6):p1649-1660 1995
ISSN: 0002-9440

10/3/24 (Item 24 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

10173989 BIOSIS NO.: 199698628907
The receptor tyrosine kinase TIE is required for integrity and survival of vascular **endothelial cells**.

AUTHOR: Puri Mira C; Rossant Janet; Alitalo Kari; Bernstein Alan; Partanen Juha(a)
AUTHOR ADDRESS: (a)Program Molecular Biology, Samuel Lunenfeld Res. Inst., Mount Sinai Hosp., 600 University Avenue, Canada

JOURNAL: EMBO (European Molecular Biology Organization) Journal 14 (23):p 5884-5891 1995
ISSN: 0261-4189

10/3/25 (Item 25 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

10169132 BIOSIS NO.: 199698624050
Dose-dependent induction of **endothelial cells** from embryonic **stem cells** using vascular permeability factor (VPF/VEGF).

AUTHOR: Reimer C L; Van De Water L
AUTHOR ADDRESS: Dep. Pathol., Beth Israel Hosp., Harv. Med. Sch., Boston, MA, USA

JOURNAL: Molecular Biology of the Cell 6 (SUPPL.):p10A 1995
ISSN: 1059-1524

10/3/26 (Item 26 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

10059400 BIOSIS NO.: 199598514318
Cloning and functional analysis of the promoter for KDR/flk-1, a receptor for vascular **endothelial** growth factor.

AUTHOR: Patterson Cam; Perrella Mark A; Hsieh Chung-Ming; Yoshizumi Masao; Lee Mu-En; Haber Edgar(a)
AUTHOR ADDRESS: (a)Build. 2, Cardiovascular Biol. Lab., Harvard Sch. Public Health, 677 Huntington Ave., Boston, MA, USA

JOURNAL: Journal of Biological Chemistry 270 (39):p23111-23118 1995
ISSN: 0021-9258

10/3/27 (Item 27 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

09947998 BIOSIS NO.: 199598402916
Failure of blood-island formation and vasculogenesis in Flk-1-deficient mice.

AUTHOR: Shalaby Fouad; Rossant Janet(a); Yamaguchi Terry P; Gertsenstein Marina; Wu Xiang-Fu; Breitman Martin L; Schuh Andre C
AUTHOR ADDRESS: (a)Samuel Lunenfeld Res. Inst., Mount Sinai Hosp., 600 University Avenue, Toronto, ON M5G 1X5, Canada

JOURNAL: Nature (London) 376 (6535):p62-66 1995
ISSN: 0028-0836

10/3/28 (Item 28 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

09875469 BIOSIS NO.: 199598330387
Angiogenic properties of human immunodeficiency virus type 1 Tat protein.

AUTHOR: Albini Adriana; Barillari Giovanni; Benelli Roberto; Gallo Robert C ; Ensoli Barbar(a)
AUTHOR ADDRESS: (a)Lab. Tumor Cell Biol., Build. 37, Room 6A09, Natl. Cancer Inst., 37 Convent Drive, Bethesda, MD , USA

JOURNAL: Proceedings of the National Academy of Sciences of the United States of America 92 (11):p4838-4842 1995
ISSN: 0027-8424

10/3/29 (Item 29 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

09734574 BIOSIS NO.: 199598189492
Increased **Stem Cell** Factor Release by Hemangioma-Derived **Endothelial Cells**.

AUTHOR: Meininger C J(a); Brightman S E; Kelly K A; Zetter B R
AUTHOR ADDRESS: (a)Dep. Med. Physiol., Texas A and M Univ. Health Sci. Cent., Reynolds Medical Build., Room 345, Co, USA

JOURNAL: Laboratory Investigation 72 (2):p166-173 1995
ISSN: 0023-6837

10/3/30 (Item 30 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

09701555 BIOSIS NO.: 199598156473
Differential **endothelial** staining of the human hematopoietic **progenitor** cell antigen (CD34) and factor VIII antigen: Utility in microvessel (**angiogenesis**) identification in bladder carcinoma.

AUTHOR: Bochner B H; Nichols P W; Groshen S; Skinner D G; Cote R J
AUTHOR ADDRESS: Los Angeles, CA, USA

JOURNAL: Modern Pathology 8 (1):p73A 1995

ISSN: 0893-3952

10/3/31 (Item 31 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

09633882 BIOSIS NO.: 199598088800
Transformation of fibroblasts into **endothelial cells** during **angiogenesis**.

AUTHOR: Kon Kazunori; Fujiwara Takashi(a)
AUTHOR ADDRESS: (a)Lab. Animal Center, Sch. Med., Ehime Univ., Shigenobu, Ehime 791-02, Japan

JOURNAL: Cell & Tissue Research 278 (3):p625-628 1994
ISSN: 0302-766X

10/3/32 (Item 32 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

09181676 BIOSIS NO.: 199497190046
B94, a primary response gene inducible by tumor necrosis factor-alpha, is expressed in developing hematopoietic tissues and the sperm acrosome.

AUTHOR: Wolf Frederick W; Sarma Vidya; Sweldin Michael; Drake Sandra; Suchard Suzanne J; Shao Haining; O'Shea K Sue; Dixit Vishva M(a)
AUTHOR ADDRESS: (a)Univ. Michigan Med. Sch., Dep. Pathol., 1301 Catherine St., Ann Arbor, MI 48109-0602, USA

JOURNAL: Journal of Biological Chemistry 269 (5):p3633-3640 1994
ISSN: 0021-9258

10/3/33 (Item 33 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

09169851 BIOSIS NO.: 199497178221
Therapeutic **angiogenesis**: A single intraarterial bolus of vascular **endothelial** growth factor augments revascularization in a rabbit **ischemic** hind limb model.

AUTHOR: Takeshita Satoshi; Zheng Lu P; Brogi Edi; Kearney Marianne; Pu Li-Qun; Bunting Stuart; Ferrara Napoleone; Symes James F; Isner Jeffrey M (a)
AUTHOR ADDRESS: (a)St. Elizabeth's Medical Cent., 736 Cambridge St., Boston, MA 02135, USA

JOURNAL: Journal of Clinical Investigation 93 (2):p662-670 1994
ISSN: 0021-9738

10/3/34 (Item 34 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

09156244 BIOSIS NO.: 199497164614
Regulation of vasculogenesis and **angiogenesis**.

AUTHOR: Risau Werner
AUTHOR ADDRESS: Max-Planck-Inst., D-61231 Bad Nauheim, Germany

JOURNAL: Journal of Cellular Biochemistry Supplement 0 (18 PART A):p260 1994
ISSN: 0733-1959

10/3/35 (Item 35 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

09118512 BIOSIS NO.: 199497126882
Early blood-brain barrier changes in the rat following transient complete cerebral **ischemia** induced by cardiac arrest.

AUTHOR: Pluta R(a); Lossinsky A S; Wisniewski H M; Mossakowski M J
AUTHOR ADDRESS: (a)Dep. Neuropathol., Med. Research Centre, Polish Acad. Sci., Dworkowa Str. 3, 00-784 Warsaw, Poland

JOURNAL: Brain Research 633 (1-2):p41-52 1994
ISSN: 0006-8993

10/3/36 (Item 36 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

08926027 BIOSIS NO.: 199396077528
Endothelial transdifferentiated phenotype and **cell**-cycle kinetics of AIDS-associated Kaposi sarcoma cells.

AUTHOR: Way D L; Witte Marlys H(a); Fiala M; Ramirez G; Nagle R B; Bernas M J; Dictor M; Borgs P; Witte C L
AUTHOR ADDRESS: (a)Univ. Ariz., Coll. Med., 1501 N. Campbell Ave., Tucson, AZ 85724, USA

JOURNAL: Lymphology 26 (2):p79-89 1993
ISSN: 0024-7766

10/3/37 (Item 37 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

08911564 BIOSIS NO.: 199396063065
Flk-1, an flt-related receptor tyrosine kinase is an early marker for **endothelial cell** precursors.

AUTHOR: Yamaguchi Terry P(a); Dumont Daniel J; Conlon Ronald A; Breitman Martin L; Rossant Janet
AUTHOR ADDRESS: (a)Samuel Lunenfeld Res. Inst., Mount Sinai Hosp., Toronto, ON, Can., M5G 1X5, SA

JOURNAL: Development (Cambridge) 118 (2):p489-498 1993
ISSN: 0950-1991

10/3/38 (Item 38 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

08850311 BIOSIS NO.: 199396001812
High affinity VEGF binding and developmental expression suggest Flk-1 as a major regulator of vasculogenesis and **angiogenesis**.

AUTHOR: Millauer Birgit(a); Wizigmann-Voos Susanne; Schnurch Harald; Martinez Ricardo; Moller Niels Peter H(a); Risau Werner; Ullrich Axel(a)

AUTHOR ADDRESS: (a)Dep. Molecular Biol., Max Planck Institute Biochemistry, An Klopferspitz 18A, 8033 Martinsried, Germany

JOURNAL: Cell 72 (6):p835-846 1993
ISSN: 0092-8674

10/3/39 (Item 1 from file: 72)
DIALOG(R)File 72:EMBASE

10893111 EMBASE No: 98336497
Paracrine PDGF-B/PDGF-Rbeta signaling controls mesangial cell development in kidney glomeruli
Lindahl P.; Hellstrom M.; Kalen M.; Karlsson L.; Pekny M.; Pekna M.; Soriano P.; Betsholtz C.
C. Betsholtz, Department of Medical Biochemistry, Goteborg University, PO Box 440, SE-405 30 Goteborg Sweden
Development (United Kingdom) , 1998, 125/17 (3313-3322)
CODEN: DEVPE ISSN: 0950-1991
DOCUMENT TYPE: Journal ; Article
LANGUAGES: ENGLISH SUMMARY LANGUAGES: ENGLISH
NUMBER OF REFERENCES: 51

10/3/40 (Item 2 from file: 72)
DIALOG(R)File 72:EMBASE

10888642 EMBASE No: 98325524
Mast cells can secrete vascular permeability factor/vascular **endothelial cell** growth factor and exhibit enhanced release after immunoglobulin E- dependent upregulation of Fcepsilon receptor I expression
Boesiger J.; Tsai M.; Maurer M.; Yamaguchi M.; Brown L.F.; Claffey K.P.; Dvorak H.F.; Galli S.J.
S.J. Galli, Department of Pathology, B. Israel Deaconess Med. Center-East, P.O. Box 15707, Boston, MA 02215 United States
Journal of Experimental Medicine (United States) , 1998, 188/6 (1135-1145)
CODEN: JEMEA ISSN: 0022-1007
PUBLICATION DATE: 19980921
DOCUMENT TYPE: Journal ; Article
LANGUAGES: ENGLISH SUMMARY LANGUAGES: ENGLISH
NUMBER OF REFERENCES: 43

10/3/41 (Item 3 from file: 72)
DIALOG(R)File 72:EMBASE

10881374 EMBASE No: 98320586
Primary pulmonary hypertension between inflammation and cancer
Voelkel N.F.; Cool C.; Lee S.D.; Wright L.; Geraci M.W.; Tuder R.M.
Dr. N.F. Voelkel, Univ. of Colorado Health Science Ctr, Box C-272, Denver, CO 80262 United States
Chest (United States) , 1998, 114/3 SUPPL. (225S-230S)
CODEN: CHETB ISSN: 0012-3692
DOCUMENT TYPE: Journal ; Conference Paper
LANGUAGES: ENGLISH SUMMARY LANGUAGES: ENGLISH
NUMBER OF REFERENCES: 35

10/3/42 (Item 4 from file: 72)
DIALOG(R)File 72:EMBASE

10808057 EMBASE No: 98241109
Role of endothelium in the control of mouse yolk sac **stem** cell differentiation
Auerbach R.; Wang S.-J.; Yu D.; Gilligan B.; Lu L.-S.
Dr. R. Auerbach, Laboratory of Developmental Biology, University of Wisconsin, 1117 W. Johnson Street, Madison, WI 53706 United States
Developmental and Comparative Immunology (United Kingdom) , 1998, 22/3 (333-338)
CODEN: DCIMD ISSN: 0145-305X
PUBLISHER ITEM IDENTIFIER: S0145305X98000056
DOCUMENT TYPE: Journal ; Review
LANGUAGES: ENGLISH SUMMARY LANGUAGES: ENGLISH
NUMBER OF REFERENCES: 14

10/3/43 (Item 5 from file: 72)
DIALOG(R)File 72:EMBASE

10808056 EMBASE No: 98241108
Hematopoietic tissues, as a playground of receptor tyrosine kinases of the PDGF-receptor family
Yoshida H.; Takakura N.; Hirashima M.; Kataoka H.; Tsuchida K.; Nishikawa S.; Nishikawa S.-I.
S.-I. Nishikawa, Department of Molecular Genetics, Faculty of Medicine, Kyoto University, Shogoin-Kawaharacho 53, Sakyo-ku, Kyoto 606-01 Japan
Developmental and Comparative Immunology (United Kingdom) , 1998, 22/3 (321-332)
CODEN: DCIMD ISSN: 0145-305X
PUBLISHER ITEM IDENTIFIER: S0145305X98000081
DOCUMENT TYPE: Journal ; Review
LANGUAGES: ENGLISH SUMMARY LANGUAGES: ENGLISH
NUMBER OF REFERENCES: 56

10/3/44 (Item 6 from file: 72)
DIALOG(R)File 72:EMBASE

10808055 EMBASE No: 98241107
Antigenic profiles of **endothelial** and hemopoietic lineages in murine intraembryonic hemogenic sites
Garcia-Porrero J.A.; Manaia A.; Jimeno J.; Lasky L.L.; Dieterlen-Lievre F.; Godin I.E.
Dr. I.E. Godin, Institut d'Embryologie Cell./Molec., CNRS, College de France, 49 bis, Avenue de la Belle Gabrielle, 94736 Nogent sur Marne, Cedex France
Developmental and Comparative Immunology (United Kingdom) , 1998, 22/3 (303-319)
CODEN: DCIMD ISSN: 0145-305X
PUBLISHER ITEM IDENTIFIER: S0145305X98000068
DOCUMENT TYPE: Journal ; Article
LANGUAGES: ENGLISH SUMMARY LANGUAGES: ENGLISH
NUMBER OF REFERENCES: 53

10/3/45 (Item 7 from file: 72)
DIALOG(R)File 72:EMBASE

10800149 EMBASE No: 98242087
The SCL gene specifies haemangioblast development from early mesoderm
Gering M.; Rodaway A.R.F.; Gottgens B.; Patient R.K.; Green A.R.

A.R. Green, University of Cambridge, Department of Haematology, MRC Centre, Hills Road, Cambridge CB2 2QH United Kingdom
EMBO Journal (United Kingdom) , 1998, 17/14 (4029-4045)
CODEN: EMJOD ISSN: 0261-4189
PUBLICATION DATE: 19980715
DOCUMENT TYPE: Journal ; Article
LANGUAGES: ENGLISH SUMMARY LANGUAGES: ENGLISH
NUMBER OF REFERENCES: 84

10/3/46 (Item 8 from file: 72)
DIALOG(R)File 72:EMBASE

10606316 EMBASE No: 98033648
Hex: A homeobox gene revealing peri-implantation asymmetry in the mouse embryo and an early transient marker of **endothelial cell** precursors
Thomas P.Q.; Brown A.; Beddington R.S.P.
R.S.P. Beddington, MRC National Institute Medical Res., The Ridgeway, London NW7 1AA United Kingdom
Development (United Kingdom) , 1998, 125/1 (85-94)
CODEN: DEVPE ISSN: 0950-1991
DOCUMENT TYPE: Journal ; Article
LANGUAGES: ENGLISH SUMMARY LANGUAGES: ENGLISH
NUMBER OF REFERENCES: 62

10/3/47 (Item 9 from file: 72)
DIALOG(R)File 72:EMBASE

10582314 EMBASE No: 98009887
TAL1/SCL is expressed in **endothelial progenitor cells** /angioblasts and defines a dorsal-to-ventral gradient of vasculogenesis
Drake C.J.; Brandt S.J.; Trusk T.C.; Little C.D.
C.J. Drake, Department of Cell Biology, Cardiovasc. Devtl. Biology Center, Medical University of South Carolina, Charleston, SC 29425 United States
Developmental Biology (United States) , 1997, 192/1 (17-30)
CODEN: DEBIA ISSN: 0012-1606
DOCUMENT TYPE: Journal ; Article
LANGUAGES: ENGLISH SUMMARY LANGUAGES: ENGLISH
NUMBER OF REFERENCES: 50

10/3/48 (Item 10 from file: 72)
DIALOG(R)File 72:EMBASE

10578058 EMBASE No: 98011115
Expression of natriuretic peptide system during embryonic **stem** cell vasculogenesis
Doi K.; Itoh H.; Nakagawa O.; Igaki T.; Yamashita J.; Chun T.-H.; Inoue M.; Masatsugu K.; Nakao K.
H. Itoh, Department Medicine Clinical Science, Kyoto University, Graduate School of Medicine, 54 Shogoin Kawahara-cho, Sakyo-ku, Kyoto 606 Japan
Heart and Vessels (Japan) , 1997, 12/SUPPL. 12 (18-22)
CODEN: HEVEE ISSN: 0910-8327
DOCUMENT TYPE: Journal ; Conference Paper
LANGUAGES: ENGLISH SUMMARY LANGUAGES: ENGLISH
NUMBER OF REFERENCES: 27

10/3/49 (Item 11 from file: 72)

DIALOG(R)File 72:EMBASE
(c) 1998 Elsevier Science B.V. All rts. reserv.

10560410 EMBASE No: 97372657
A requirement for Flk1 in primitive and definitive hematopoiesis and vasculogenesis
Shalaby F.; Ho J.; Stanford W.L.; Fischer K.-D.; Schuh A.C.; Schwartz L.; Bernstein A.; Rossant J.
F. Shalaby, Samuel Lunenfeld Research Institute, Mount Sinai Hospital, 600 University Avenue, Toronto, Ont. M5G 1X5 Canada
Cell (USA) , 1997, 89/6 (981-990)
CODEN: CELLB ISSN: 0092-8674
DOCUMENT TYPE: Journal
LANGUAGES: English SUMMARY LANGUAGES: English
NUMBER OF REFERENCES: 61

10/3/50 (Item 12 from file: 72)
DIALOG(R)File 72:EMBASE
(c) 1998 Elsevier Science B.V. All rts. reserv.

10540953 EMBASE No: 97358521
Eph family receptors and ligands in vascular cell targeting and assembly
Stein E.; Schoecklmann H.; Daniel T.O.
E. Stein, Department of Pharmacology, Vanderbilt University Medical Center, Nashville, TN USA
Trends in Cardiovascular Medicine (USA) , 1997, 7/8 (329-334)
CODEN: TCMDE ISSN: 1050-1738
DOCUMENT TYPE: Journal
LANGUAGES: English SUMMARY LANGUAGES: English
NUMBER OF REFERENCES: 52

10/3/51 (Item 13 from file: 72)
DIALOG(R)File 72:EMBASE
(c) 1998 Elsevier Science B.V. All rts. reserv.

10520547 EMBASE No: 97331947
Immunoreactivity patterns of CD31 and CD68 in 28 cases of Kaposi's sarcoma: Evidence supporting **endothelial** differentiation in the spindle **cell** component
Hoerl H.D.; Goldblum J.R.
Dr. J.R. Goldblum, Cleveland Clinic Foundation, 9500 Euclid Avenue L25, Cleveland, OH USA
Applied Immunohistochemistry (USA) , 1997, 5/3 (173-178)
CODEN: APIME ISSN: 1062-3345
DOCUMENT TYPE: Journal
LANGUAGES: English SUMMARY LANGUAGES: English
NUMBER OF REFERENCES: 46

10/3/52 (Item 14 from file: 72)
DIALOG(R)File 72:EMBASE
(c) 1998 Elsevier Science B.V. All rts. reserv.

10518727 EMBASE No: 97318362
Integrin is essential for teratoma growth and **angiogenesis**
Bloch W.; Forsberg E.; Lentini S.; Brakebusch C.; Martin K.; Krell H.W.; Weidle U.H.; Addicks K.; Fassler R.
R. Fassler, Max Planck Institut fur Biochemie, am Klopferspitz 18 A, 82 152 Martinstied Germany
Journal of Cell Biology (USA) , 1997, 139/1 (265-278)
CODEN: JCLBA ISSN: 0021-9525
DOCUMENT TYPE: Journal
LANGUAGES: English SUMMARY LANGUAGES: English

NUMBER OF REFERENCES: 38

10/3/53 (Item 15 from file: 72)
DIALOG(R)File 72:EMBASE

10409080 EMBASE No: 97213623
Regulation of tie receptor expression on human **endothelial cells** by protein kinase C-mediated release of soluble tie
Yabkowitz R.; Meyer S.; Yanagihara D.; Brankow D.; Staley T.; Elliott G.; Hu S.; Ratzkin B.
Dr. R. Yabkowitz, Mammalian Cell Molecular Biology, M/S 14-2-C, Amgen Inc, 1840 DeHavilland Dr, Thousand Oaks, CA 91320-1789 USA
Blood (USA) , 1997, 90/2 (706-715)
CODEN: BLOOA ISSN: 0006-4971
DOCUMENT TYPE: Journal
LANGUAGES: English SUMMARY LANGUAGES: English
NUMBER OF REFERENCES: 49

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DIALOG(R)File 72:EMBASE

10380319 EMBASE No: 97192043
Targeted null-mutation in the vascular **endothelial**-cadherin gene impairs the organization of vascular-like structures in embryoid bodies
Vittet D.; Buchou T.; Schweitzer A.; Dejana E.; Huber P.
D. Vittet, Commissariat a l'Energie Atomique, Laboratoire d'Hematologie, INSRM U217, 17 rue des Martyrs, 38054 Grenoble Cedex 9 France
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CODEN: PNASA ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGES: English SUMMARY LANGUAGES: English
NUMBER OF REFERENCES: 54

10/3/55 (Item 17 from file: 72)
DIALOG(R)File 72:EMBASE

10354907 EMBASE No: 97152440
A role for notochord in axial vascular development revealed by analysis of phenotype and the expression of VEGR-2 in zebrafish flh and ntl mutant embryos
Sumoy L.; Bennett Keasey J.; Dittman T.D.; Kimelman D.
D. Kimelman, Department Biochemistry, University of Washington, Seattle, WA 98195-7350 USA
Mechanisms of Development (Ireland) , 1997, 63/1 (15-27)
CODEN: MEDVE ISSN: 0925-4773
PUBLISHER ITEM IDENTIFIER: S0925477397006710
DOCUMENT TYPE: Journal
LANGUAGES: English SUMMARY LANGUAGES: English
NUMBER OF REFERENCES: 62

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DIALOG(R)File 72:EMBASE

10331478 EMBASE No: 97145315
Human cytotrophoblasts adopt a vascular phenotype as they differentiate: A strategy for successful endovascular invasion?

Zhou Y.; Fisher S.J.; Janatpour M.; Genbacev O.; Dejana E.; Wheelock M.; Damsky C.H.
USA
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CODEN: JCINA ISSN: 0021-9738
DOCUMENT TYPE: Journal
LANGUAGES: English SUMMARY LANGUAGES: English
NUMBER OF REFERENCES: 48

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DIALOG(R)File 72:EMBASE
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10168376 EMBASE No: 96348565
Erythropoiesis and vasculogenesis in embryoid bodies lacking visceral yolk sac endoderm
Bielinska M.; Narita N.; Heikinheimo M.; Porter S.B.; Wilson D.B.
Department of Pediatrics, Washington Univ. School of Medicine, St. Louis Children's Hospital, One Children's Place, St Louis, MO 63110 USA
Blood (USA) , 1996, 88/10 (3720-3730)
CODEN: BLOOA ISSN: 0006-4971
LANGUAGES: English SUMMARY LANGUAGES: English

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10097003 EMBASE No: 96288421
Flk-1, a receptor for vascular **endothelial** growth factor (VEGF), is expressed by retinal **progenitor** cells
Yang X.; Cepko C.L.
Department of Genetics, Howard Hughes Medical Institute, Harvard Medical School, Boston, MA 02115 USA
Journal of Neuroscience (USA) , 1996, 16/19 (6089-6099)
CODEN: JNRSD ISSN: 0270-6474
LANGUAGES: English SUMMARY LANGUAGES: English

10/3/59 (Item 21 from file: 72)
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10041079 EMBASE No: 96233379
Induction of embryonic vasculogenesis by bFGF and LIF in vitro and in vivo
Gendron R.L.; Tsai F.-Y.; Paradis H.; Arceci R.J.
Department of Pediatrics, Division of Hematology and Oncology, Child. Hospital Research Foundation, 3333 Burnet Avenue, Cincinnati, OH 45229-3039 USA
Developmental Biology (USA) , 1996, 177/1 (332-346)
CODEN: DEBIA ISSN: 0012-1606
LANGUAGES: English SUMMARY LANGUAGES: English

10/3/60 (Item 22 from file: 72)
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9979409 EMBASE No: 96164968
Two distinct **endothelial** lineages in ontogeny, one of them related to hemopoiesis
Pardanaud L.; Luton D.; Prigent M.; Bourcheix L.-M.; Catala M.; Dieterlen-Lievre F.

Inst. Embryologie Cell. Moleculaire, CNRS, College de France, Ave. de la Belle Gabrielle, 94736 Nogent-sur-Marne Cedex France
Development (United Kingdom) , 1996, 122/5 (1363-1371)
CODEN: DEVPE ISSN: 0950-1991
LANGUAGES: English SUMMARY LANGUAGES: English

10/3/61 (Item 23 from file: 72)
DIALOG(R)File 72:EMBASE

9922963 EMBASE No: 96108150
Abnormal blood vessel development and lethality in embryos lacking a single VEGF allele
Carmeliet P.; Ferreira V.; Breier G.; Pollefeyt S.; Kieckens L.; Gertenstein M.; Fahrig M.; Vandenhoeck A.; Harpal K.; Eberhardt C.; Decleucq C.; Pawling J.; Moons L.; Collen D.; Risau W.; Nagy A.
Ctr. Transgene Technol. Gene Therapy, Flanders Interuniversity, Institute for Biotechnology, B-3000 Leuven Belgium
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CODEN: NATUA ISSN: 0028-0836
LANGUAGES: English SUMMARY LANGUAGES: English

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9903349 EMBASE No: 96085813
Brainstem **ischemic** damage following occlusion of the blood vessels in the rat's posterior cerebral circulation
Inui H.; Murai T.; Yane K.; Matsunaga T.
Department of Otorhinolaryngology, Nara Medical College, 840 Shijo-cho Kashihara City, Nara 634 Japan
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CODEN: EAOTE ISSN: 0937-4477
LANGUAGES: English SUMMARY LANGUAGES: English

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9826454 EMBASE No: 96007672
Blood island formation in attached cultures of murine embryonic **stem** cells
Bautch V.L.; Stanford W.L.; Rapoport R.; Russell S.; Byrum R.S.; Futch T.A.
Dept. of Biology, University of North Carolina, CB 3280, Chapel Hill, NC 27599 USA
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CODEN: DEDYE ISSN: 1058-8388
LANGUAGES: English SUMMARY LANGUAGES: English

10/3/64 (Item 26 from file: 72)
DIALOG(R)File 72:EMBASE

9811259 EMBASE No: 95367134
Time course of increased cellular proliferation collateral arteries after administration of vascular **endothelial** growth factor in a rabbit model of lower limb vascular insufficiency
Takeshita S.; Rossow S.T.; Kearney M.; Zheng L.P.; Bauters C.; Bunting S.

; Ferrara N.; Symes J.F.; Isner J.M.
St. Elizabeths Medical Center, 736 Cambridge Street, Boston, MA 02135 USA
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CODEN: AJPAA ISSN: 0002-9440
LANGUAGES: English SUMMARY LANGUAGES: English

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9595450 EMBASE No: 95166035
Pathology of the liver
Lefkowitch J.H.
Department of Pathology, College of Physicians and Surgeons, Columbia University, PH15 West, 630 West 168th Street, New York, NY 10032 USA
Current Opinion in Gastroenterology (United Kingdom) , 1995, 11/3 (195-201)
CODEN: COGAE ISSN: 0267-1379
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9329688 EMBASE No: 94279673
Dominant-negative and targeted null mutations in the **endothelial** receptor tyrosine kinase, tek, reveal a critical role in vasculogenesis of the embryo
Dumont D.J.; Gradwohl G.; Fong G.-H.; Puri M.C.; Gertsenstein M.; Auerbach A.; Breitman M.L.
Molecular/Developmental Biology Div., Samuel Lunenfeld Research Institute, Mount Sinai Hospital, Toronto, Ont. Canada
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LANGUAGES: English SUMMARY LANGUAGES: English

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DIALOG(R)File 72:EMBASE

9258185 EMBASE No: 94206283
Heparin modulates the interaction of VEGF165 with soluble and cell associated flk-1 receptors
Tessler S.; Rockwell P.; Hicklin D.; Cohen T.; Levi B.-Z.; Witte L.; Lemischka I.R.; Neufeld G.
Department of Biology, Israel Institute of Technology, Haifa 32000 Israel
J. BIOL. CHEM. (USA) , 1994, 269/17 (12456-12461)
CODEN: JBCHA ISSN: 0021-9258
LANGUAGES: English SUMMARY LANGUAGES: English

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9209096 EMBASE No: 94147090
Myogenic cells in the rat embryonic brain **stem**
De Vitry F.; Hillion J.; Catelon J.; Gros F.
Laboratoire de Biochimie Cellulaire, CNRS-URA 1115, College de France, 11, Place Marcelin Berthelot, 75231 Paris Cedex 05 France

C. R. ACAD. SCI. SER. III (France) , 1994, 317/4 (332-340)
CODEN: CRASE ISSN: 0764-4469
LANGUAGES: English SUMMARY LANGUAGES: English; French

10/3/69 (Item 31 from file: 72)
DIALOG(R)File 72:EMBASE

8988412 EMBASE No: 93292184
Embryonic **stem** cell model systems for vascular morphogenesis and cardiac disorders
Doetschman T.; Shull M.; Kier A.; Coffin J.D.
Department of Molecular Genetics, Cincinnati Univ. College of Medicine, Cincinnati, OH 45267-0524 USA
HYPERTENSION (USA) , 1993, 22/4 (618-629)
CODEN: HPRTD ISSN: 0194-911X
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10/3/70 (Item 32 from file: 72)
DIALOG(R)File 72:EMBASE

8956241 EMBASE No: 93259964
Development of human peribiliary capillary plexus: A lectin-histochemical and immunohistochemical study
Terada T.; Nakanuma Y.
Second Department of Pathology, Kanazawa University Sch. of Medicine, Kanazawa 920 Japan
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CODEN: HPTLD ISSN: 0270-9139
LANGUAGES: English SUMMARY LANGUAGES: English

10/3/71 (Item 33 from file: 72)
DIALOG(R)File 72:EMBASE

8910279 EMBASE No: 93214049
Flk-1, an fit-related receptor tyrosine kinase is an early marker for **endothelial cell** precursors
Yamaguchi T.P.; Dumont D.J.; Conlon R.A.; Breitman M.L.; Rossant J.
Samuel Lunenfeld Research Instltute, Mount Sinai Hospital, Toronto, Ont. M5G 1X5 Canada
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CODEN: DEVPE ISSN: 0950-1991
LANGUAGES: English SUMMARY LANGUAGES: English

10/3/72 (Item 34 from file: 72)
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8821673 EMBASE No: 93125395
Embryology of the vascular system
L'EMBRYOLOGIE DES VAISSEAUX
Dieterlen-Lievre F.; Pardanaud L.
Inst. d'Embryol. Cellulaire/Molecul., CNRS, College de France, 49 bis, Avenue de la Belle-Gabrielle, F-94736 Nogent-sur-Marne Cedex France
ANN. CARDIOL. ANGEIOL. (France) , 1993, 42/2 (A.5-A.12)
CODEN: ACAAB ISSN: 0003-3928
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10/3/73 (Item 35 from file: 72)
DIALOG(R)File 72:EMBASE

8643755 EMBASE No: 92324311
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Mikawa T.; Fischman D.A.
Department of Cell Biology/Anatomy, Cornell University Medical College, 1300 York Avenue, New York, NY 10021 USA
PROC. NATL ACAD. SCI. U. S. A. (USA) , 1992, 89/20 (9504-9508)
CODEN: PNASA ISSN: 0027-8424
LANGUAGES: English SUMMARY LANGUAGES: English

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7790231 EMBASE No: 90219551
Leukocyte antigen CD34 is expressed by a subset of cultured **endothelial cells** and on **endothelial** abluminal microprocesses in the tumor stroma
Schlingemann R.O.; Rietveld F.J.R.; De Waal R.M.W.; Bradley N.J.; Skene A.I.; Davies A.J.S.; Greaves M.F.; Denekamp J.; Ruiter D.J.
Department of Pathology, University Hospital Nijmegen, P.O. Box 9101, 6500 HB Nijmegen Netherlands
LAB. INVEST. (USA) , 1990, 62/6 (690-696)
CODEN: LAINA ISSN: 0023-6837
LANGUAGES: English

10/3/75 (Item 37 from file: 72)
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7376610 EMBASE No: 89093194
Relationship between vasculogenesis, **angiogenesis** and haemopoiesis during avian ontogeny
Pardanaud L.; Yassine F.; Dieterlen-Lievre F.
Institut d'Embryologie Cellulaire et Moleculaire du CNRS et du College de France, 94736 Nogent sur Marne Cedex France
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LANGUAGES: English

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7087792 EMBASE No: 88084930
Vasculogenesis and **angiogenesis** in embryonic-**stem** -cell-derived embryoid bodies
Risau W.; Sariola H.; Zerwes H.-G.; Sasse J.; Ekblom P.; Kemler R.; Doetschman T.
Max-Planck-Institut fur Entwicklungsbiologie, 7400 Tubingen Germany, Federal Republic of
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LANGUAGES: English

10/3/77 (Item 1 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

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09569375 98295994
The chemokine receptor CXCR4 is essential for vascularization of the gastrointestinal tract [see comments]
Tachibana K; Hirota S; Iizasa H; Yoshida H; Kawabata K; Kataoka Y; Kitamura Y; Matsushima K; Yoshida N; Nishikawa S; Kishimoto T; Nagasawa T
Department of Immunology, Research Institute, Osaka Medical Center for Maternal and Child Health, Izumi, Japan.
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Languages: ENGLISH
Document type: JOURNAL ARTICLE

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DIALOG(R)File 154:MEDLINE(R)
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Avian VEGF-C: cloning, embryonic expression pattern and stimulation of the differentiation of VEGFR2-expressing **endothelial cell** precursors.
Eichmann A; Corbel C; Jaffredo T; Breant C; Joukov V; Kumar V; Alitalo K; le Douarin NM
Institut d'Embryologie Cellulaire et Moleculaire du CNRS et du College de France, Nogent-sur-Marne, France. eichmann@infobiogen.fr
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Languages: ENGLISH
Document type: JOURNAL ARTICLE

10/3/79 (Item 3 from file: 154)
DIALOG(R)File 154:MEDLINE(R)
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Basic fibroblast growth factor downregulates Bcl-2 and promotes apoptosis in MCF-7 human breast cancer cells.
Wang Q; Maloof P; Wang H; Fenig E; Stein D; Nichols G; Denny TN; Yahalom J; Wieder R
Department of Medicine, UMDNJ-New Jersey Medical School, Newark 07103 USA.
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Languages: ENGLISH
Document type: JOURNAL ARTICLE

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DIALOG(R)File 154:MEDLINE(R)
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Differential expression and biological activity of the heparin-binding growth-associated molecule (HB-GAM) in lung cancer cell lines.
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Department of Hematology/Oncology, Philipps-Universitat, Marburg, Germany.
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DIALOG(R)File 154:MEDLINE(R)

09255338 97126252
Inhibition of **angiogenesis** in human glioblastomas by chromosome 10 induction of thrombospondin-1.
Hsu SC; Volpert OV; Steck PA; Mikkelsen T; Polverini PJ; Rao S; Chou P; Bouck NP
Department of Microbiology-Immunology, R.H. Lurie Cancer Center, Northwestern University Medical School, Chicago, Illinois 60611, USA.
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Contract/Grant No.: CA52750, CA, NCI; CA56041, CA, NCI; HL39926, HL, NHLBI
Languages: ENGLISH
Document type: JOURNAL ARTICLE

10/3/82 (Item 6 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

09183575 97454183
Comparison of biological phenotypes according to midkine expression in gastric cancer cells and their autocrine activities could be modulated by pentosan polysulfate.
Rha SY; Noh SH; Kwak HJ; Wellstein A; Kim JH; Roh JK; Min JS; Kim BS; Chung HC
Yonsei Cancer Research Institute, Yonsei University College of Medicine, Seoul, South Korea.
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Languages: ENGLISH
Document type: JOURNAL ARTICLE

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Lindahl P; Johansson BR; Leveen P; Betsholtz C
Department of Medical Biochemistry, University of Goteborg, Medicinaregatan 9A, S-413 90 Goteborg, Sweden.
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Document type: JOURNAL ARTICLE

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Colonization of neural allografts by host microglial cells: relationship to graft **neovascularization**.
Pennell NA; Streit WJ
Department of Neuroscience, University of Florida Brain Institute, Gainesville 32610, USA.
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Languages: ENGLISH
Document type: JOURNAL ARTICLE

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09026434 97286336
Vascular development: cellular and molecular regulation.
Beck L Jr; D'Amore PA
Department of Pathology, Harvard Medical School, Children's Hospital, Boston, Massachusetts 02115, USA.
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Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW; REVIEW LITERATURE

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DIALOG(R)File 154:MEDLINE(R)

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Vessel patterning in the embryo of the zebrafish: guidance by notochord.
Fouquet B; Weinstein BM; Serluca FC; Fishman MC
Cardiovascular Research Center, Massachusetts General Hospital, Charlestown 02129, USA.
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Contract/Grant No.: RO1-HL49579, HL, NHLBI; T32-HL07208, HL, NHLBI
Languages: ENGLISH
Document type: JOURNAL ARTICLE

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DIALOG(R)File 154:MEDLINE(R)

08975049 97183746
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Chang HN; Garetto LP; Katona TR; Potter RH; Roberts WE
Department of Oral Facial Development, School of Dentistry, Indiana University, Indianapolis 46202, USA.
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Languages: ENGLISH
Document type: JOURNAL ARTICLE

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DIALOG(R)File 154:MEDLINE(R)

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The **angiogenic** potentials of the cephalic mesoderm and the origin of brain and head blood vessels.
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Institut d'Embryologie Cellulaire et Moleculaire du CNRS et du College de France, UMR 9924, Nogent-sur-Marne, France.
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Document type: JOURNAL ARTICLE

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DIALOG(R)File 154:MEDLINE(R)

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Insulin stimulates the expression of basic fibroblast growth factor in rat brown adipocyte primary culture.
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Department of Hygiene, National Defense Medical College, Tokorozawa/Japan.
Eur J Cell Biol (GERMANY) Sep 1995, 68 (1) p8-13, ISSN 0171-9335 Journal Code: EM7
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Document type: JOURNAL ARTICLE

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DIALOG(R)File 154:MEDLINE(R)

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Bikfalvi A; Han ZC
INSERM U 118, Paris, France.
Leukemia (ENGLAND) Mar 1994, 8 (3) p523-9, ISSN 0887-6924 Journal Code: LEU
Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL

10/3/91 (Item 15 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

08044936 95042611
In vitro studies on the existence of **endothelial** precursor **cells** in the subectodermal avascular region of quail wing buds.
Seifert R
Ruhr-Universitat Bochum, Abteilung fur Anatomie und Embryologie, Germany.
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Contract/Grant No.: NICHD NO1-HD-2-3144, HD, NICHD
Languages: ENGLISH
Document type: JOURNAL ARTICLE

10/3/92 (Item 16 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

07925532 94259720
Apolipoprotein E: a potent inhibitor of **endothelial** and tumor **cell** proliferation.
Vogel T; Guo NH; Guy R; Drezlich N; Krutzsch HC; Blake DA; Panet A; Roberts DD
Laboratory of Pathology, National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20892.
J Cell Biochem (UNITED STATES) Mar 1994, 54 (3) p299-308, ISSN 0730-2312 Journal Code: HNF
Contract/Grant No.: R01 EY09092, EY, NEI
Languages: ENGLISH
Document type: JOURNAL ARTICLE

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DIALOG(R)File 154:MEDLINE(R)

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Developmental relationships between hemopoiesis and vasculogenesis.
Dieterlen-Lievre F; Pardanaud L; Godin I; Garcia-Porrero J; Cumano A; Marcos M
Institut d'Embryologie Cellulaire et Moleculaire du CNRS, College de France, Nogent-sur-Marne.
C R Acad Sci III (FRANCE) Sep 1993, 316 (9) p892-901, ISSN 0764-4469 Journal Code: CA1
Languages: ENGLISH, FRENCH
Document type: JOURNAL ARTICLE

10/3/94 (Item 18 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

07542369 93263568
[Embryology of vessels]
L'embryologie des vaisseaux.
Dieterlen-Lievre F; Pardanaud L
Institut d'Embryologie Cellulaire et Moleculaire du CNRS, College de France, Nogent-sur-Marne.
Ann Cardiol Angeiol (Paris) (FRANCE) Feb 1993, 42 (2) pA5-12, ISSN 0003-3928 Journal Code: 502
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Document type: JOURNAL ARTICLE English Abstract

10/3/95 (Item 19 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

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Capillary growth: a two-cell system.
D'Amore PA
Department of Surgery, Children's Hospital, Boston, MA 02115.
Semin Cancer Biol (UNITED STATES) Apr 1992, 3 (2) p49-56, ISSN 1044-579X Journal Code: A6Y
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Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL

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DIALOG(R)File 154:MEDLINE(R)

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Pericytes as a supplementary source of osteoblasts in periosteal osteogenesis.
Diaz-Flores L; Gutierrez R; Lopez-Alonso A; Gonzalez R; Varela H
Department of Pathology, La Laguna University, Canary Islands, Spain.
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Document type: JOURNAL ARTICLE

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DIALOG(R)File 154:MEDLINE(R)

07001796 91288073
[Metastatic dissemination of cancer cells]
Dissemination metastatique des cellules cancereuses.
Cornil I; Theodorescu D; Kerbel RS; Poupon MF
Samuel Lunenfeld Research Institute, Mount Sinai Hospital, Toronto, Canada.
Pathol Biol (Paris) (FRANCE) Apr 1991, 39 (4) p300-7, ISSN 0369-8114 Journal Code: OSG
Languages: FRENCH Summary Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL English Abstract

10/3/98 (Item 22 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

07001319 91277020
Extracellular matrix-resident basic fibroblast growth factor: implication for the control of **angiogenesis**.
Vlodavsky I; Fuks Z; Ishai-Michaeli R; Bashkin P; Levi E; Korner G; Bar-Shavit R; Klagsbrun M
Department of Oncology, Hadassah-Hebrew University Hospital, Jerusalem, Israel.
J Cell Biochem (UNITED STATES) Feb 1991, 45 (2) p167-76, ISSN 0730-2312 Journal Code: HNF
Contract/Grant No.: CA-30289, CA, NCI; CA-37392, CA, NCI
Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL

10/3/99 (Item 23 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

06820662 92038454
Angioblast differentiation and morphogenesis of the vascular endothelium in the mouse embryo.
Coffin JD; Harrison J; Schwartz S; Heimark R
Department of Pathology, University of Washington, Seattle 98115.
Dev Biol (UNITED STATES) Nov 1991, 148 (1) p51-62, ISSN 0012-1606 Journal Code: E7T
Contract/Grant No.: HL-18645, HL, NHLBI; HL-26405, HL, NHLBI; HL-45335-03, HL, NHLBI
Languages: ENGLISH
Document type: JOURNAL ARTICLE

10/3/100 (Item 24 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

06644411 91103064
Effects of high-dose methylprednisolone on Na(+)-K+ ATPase and lipid peroxidation after experimental subarachnoid hemorrhage.
Marzatico F; Gaetani P; Buratti E; Messina AL; Ferlenga P; Rodriguez y Baena R
Institute of Pharmacology, IRCCS Policlinico S. Matteo, University of Pavia, Italy.
Acta Neurol Scand (DENMARK) Oct 1990, 82 (4) p263-70, ISSN 0001-6314 Journal Code: 1BS
Languages: ENGLISH
Document type: JOURNAL ARTICLE

10/3/101 (Item 25 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

05959417 90094568
Early haemopoietic **stem** cells in the avian embryo.
Dieterlen-Lievre F; Pardanaud L; Yassine F; Cormier F
Institut d'embryologie Cellulaire et Moleculaire du CNRS, Nogent s/Marne, France.
J Cell Sci Suppl (ENGLAND) 1988, 10 p29-44, ISSN 0269-3518
Journal Code: HNG
Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW; REVIEW, ACADEMIC

10/3/102 (Item 26 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

05915109 90214513
Complementary patterns of expression of c-ets 1, c-myb and c-myc in the blood-forming system of the chick embryo.
Vandenbunder B; Pardanaud L; Jaffredo T; Mirabel MA; Stehelin D
Institut National de la Sante et de la Recherche Medicale, Unite 186/Centre National de la Recherche Scientifique URA 1160, Institut Pasteur, Lille, France.
Development (ENGLAND) Oct 1989, 107 (2) p265-74, ISSN 0950-1991
Journal Code: ECW
Languages: ENGLISH
Document type: JOURNAL ARTICLE

10/3/103 (Item 27 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

05910683 90041356
[Morphologic findings and biologic behavior in the high grade glioma--a postmortem study of 22 cases]
Ogashiwa M; Maeda T; Yokoyama H; Takeuchi K; Akai K
National Center of Neurology and Psychiatry.
Gan No Rinsho (JAPAN) Sep 1989, 35 (11) p1297-307, ISSN 0021-4949
Journal Code: KIF
Languages: JAPANESE Summary Languages: ENGLISH
Document type: JOURNAL ARTICLE English Abstract

10/3/104 (Item 28 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

05909243 90002309
The response of the microvascular system to radiation: a review.
Baker DG; Krochak RJ
Division of Radiation Oncology, University of Virginia Medical Center, Charlottesville 22908.
Cancer Invest (UNITED STATES) 1989, 7 (3) p287-94, ISSN 0735-7907
Journal Code: CAI
Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL

10/3/105 (Item 29 from file: 154)

DIALOG(R)File 154:MEDLINE(R)
(c) format only 1998 Dialog Corporation. All rts. reserv.

04929518 86270354
[Osteogenic precursor cells in repair osteogenesis]
K voprosu ob osteogennykh kletkakh-predshestvennikakh pri reparativnom osteogeneze.
Mikhailova LN; Pal'tsyn AA
Biull Eksp Biol Med (USSR) Jun 1986, 101 (6) p755-7, ISSN 0365-9615 Journal Code: A74
Languages: RUSSIAN Summary Languages: ENGLISH
Document type: JOURNAL ARTICLE English Abstract

10/3/106 (Item 30 from file: 154)
DIALOG(R)File 154:MEDLINE(R)
(c) format only 1998 Dialog Corporation. All rts. reserv.

04739694 86036473
Delayed CSF lavage for arteriographic and morphological vasospasm after experimental SAH.
Alexander E 3d; Black PM; Liszczak TM; Zervas NT
J Neurosurg (UNITED STATES) Dec 1985, 63 (6) p949-58, ISSN 0022-3085 Journal Code: JD3
Contract/Grant No.: NS10828, NS, NINDS; 2RO1-HI22573-08, HI, NHLBI; NS00553, NS, NINDS
Languages: ENGLISH
Document type: JOURNAL ARTICLE

10/3/107 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
(c) 1998 American Chemical Society. All rts. reserv.

129008577 CA: 129(1)8577w PATENT
Methods for regulating angiogenesis
INVENTOR(AUTHOR): Isner, Jeffrey M.; Asahara, Takayuki
LOCATION: USA
ASSIGNEE: St. Elizabeth's Medical Center of Boston, Inc.
PATENT: PCT International ; WO 9819712 A1 DATE: 19980514
APPLICATION: WO 97US19935 (19971106) *US 744882 (19961108)
PAGES: 57 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: A61K-048/00A; A61K-035/12B; C12N-005/10B; A61K-047/00B; A61K-049/00B
DESIGNATED COUNTRIES: AU; CA; JP DESIGNATED REGIONAL: AT; BE; CH; DE; DK ; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE

10/3/108 (Item 2 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
(c) 1998 American Chemical Society. All rts. reserv.

128242083 CA: 128(20)242083h JOURNAL
Endothelial progenitor cells for neovascularization
AUTHOR(S): Asahara, Takayuki; Takahashi, Tomono; Isner, Jeffery M.
LOCATION: Sch. Med., Tufts Univ., Boston, 02135, USA
JOURNAL: Jikken Igaku DATE: 1998 VOLUME: 16 NUMBER: 5 PAGES: 605-611
CODEN: JIIGEF ISSN: 0288-5514 LANGUAGE: Japanese PUBLISHER: Yodosha

10/3/109 (Item 3 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
(c) 1998 American Chemical Society. All rts. reserv.

128046126 CA: 128(5)46126k JOURNAL
Cell interactions in the mouse yolk sac: vasculogenesis and hematopoiesis

AUTHOR(S): Auerbach, Robert; Gilligan, Barbara; Lu, Li-Sheng; Wang, Shur-Jen
LOCATION: Laboratory of Developmental Biology, University of Wisconsin, Madison, WI, 53706, USA
JOURNAL: J. Cell. Physiol. DATE: 1997 VOLUME: 173 NUMBER: 2, Development, Cell Differentiation and Cancer PAGES: 202-205 CODEN: JCLLAX
ISSN: 0021-9541 LANGUAGE: English PUBLISHER: Wiley-Liss

10/3/110 (Item 4 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
(c) 1998 American Chemical Society. All rts. reserv.

127159382 CA: 127(12)159382p JOURNAL
Isolation of endothelial progenitor cell for angiogenesis
AUTHOR(S): Asahara, Takayuki
LOCATION: St. Elizabeth's Med. Cent., Tufts Univ. Sch. Med., Boston, 02135, USA
JOURNAL: Jikken Igaku DATE: 1997 VOLUME: 15 NUMBER: 12 PAGES: 1507-1510 CODEN: JIIGEF ISSN: 0288-5514 LANGUAGE: Japanese PUBLISHER: Yodosha

10/3/111 (Item 1 from file: 351)
DIALOG(R)File 351:DERWENT WPI
(c)1998 Derwent Info Ltd. All rts. reserv.

012040197
WPI Acc No: 98-457107/199839
XRAM Acc No: C98-138272
Transgenic non-human animals - which contain **cells** with modified vascular **endothelial** growth factor B gene for use in diagnostic and therapeutic studies
Patent Assignee: LUDWIG INST CANCER RES (LUDW-N)
Inventor: AASE K; BETSHOLTZ C; ERIKSSON U; GEBRE-MEDHIN S; LI X; PEKNY M; VON EULER G
Number of Countries: 022 Number of Patents: 001
Patent Family:
Patent No Kind Date Applicat No Kind Date Main IPC Week
WO 9836052 A1 19980820 WO 98US3212 A 19980218 C12N-005/00 199839 B

Priority Applications (No Type Date): US 9738202 A 19970218
Filing Details:
Patent Kind Filing Notes Application Patent
WO 9836052 A1
Designated States (National): AU CA CN JP NZ
Designated States (Regional): AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
Language, Pages: WO 9836052 (E, 44)

10/3/112 (Item 2 from file: 351)
DIALOG(R)File 351:DERWENT WPI
(c)1998 Derwent Info Ltd. All rts. reserv.

011869696
WPI Acc No: 98-286606/199825
XRAM Acc No: C98-088752
Using **endothelial progenitor cells** for therapeutic regulation of **angiogenesis** - e.g. to treat tumours of ischaemia, also for treating injured blood vessels and to detect ischaemic tissue or injured vessels in vivo
Patent Assignee: ST ELIZABETH'S MEDICAL CENT BOSTON INC (SELI-N)
Inventor: ASAHARA T; ISNER J M
Number of Countries: 020 Number of Patents: 002

Patent Family:
Patent No Kind Date Applicat No Kind Date Main IPC Week
WO 9819712 A1 19980514 WO 97US19935 A 19971106 A61K-048/00 199825 B
AU 9852432 A 19980529 AU 9852432 A 19971106 A61K-048/00 199841

Priority Applications (No Type Date): US 96744882 A 19961108
Filing Details:
Patent Kind Filing Notes Application Patent
WO 9819712 A1
Designated States (National): AU CA JP
Designated States (Regional): AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
AU 9852432 A Based on WO 9819712
Language, Pages: WO 9819712 (E, 56)

10/3/113 (Item 3 from file: 351)
DIALOG(R)File 351:DERWENT WPI
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011834381
WPI Acc No: 98-251291/199822
XRAM Acc No: C98-078406
New fibroblast growth factor homologue, zFGF-5 - used to develop products for treating e.g. heart failure, stroke, hypertension, bone defects or cancers, arthritis, or wounds
Patent Assignee: ZYMOGENETICS INC (ZYMO)
Inventor: BUKOWSKI T R; CONKLIN D C; DEISHER T A; HANSEN B; HOLDERMAN S D; RAYMOND F C; SHEPPARD P O
Number of Countries: 075 Number of Patents: 002
Patent Family:
Patent No Kind Date Applicat No Kind Date Main IPC Week
WO 9816644 A1 19980423 WO 97US18635 A 19971016 C12N-015/18 199822 B
AU 9747583 A 19980511 AU 9747583 A 19971016 C12N-015/18 199837

Priority Applications (No Type Date): US 9628646 A 19961016
Filing Details:
Patent Kind Filing Notes Application Patent
WO 9816644 A1
Designated States (National): AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG UZ VN
Designated States (Regional): AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
AU 9747583 A Based on WO 9816644
Language, Pages: WO 9816644 (E, 94)

10/3/114 (Item 4 from file: 351)
DIALOG(R)File 351:DERWENT WPI
(c)1998 Derwent Info Ltd. All rts. reserv.

011624223
WPI Acc No: 98-041351/199804
XRAM Acc No: C98-013778
Laminin-derived peptides with cell adhesion and morphogenesis activity - for coating culture dishes, prostheses etc., also therapeutically to improve wound healing, inhibit metastasis etc.
Patent Assignee: UNIV VIRGINIA PATENT FOUND (UYVI-N)
Inventor: CHEN L; LAURIE G W; MATTER M L
Number of Countries: 001 Number of Patents: 001
Patent Family:
Patent No Kind Date Applicat No Kind Date Main IPC Week
US 5696229 A 19971209 US 95405200 A 19950316 A61K-038/03 199804 B

Priority Applications (No Type Date): US 95405200 A 19950316
Language, Pages: US 5696229 (33)
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